

US 6,951,894 B1

15

- (3) Calculate corrected concentrations of ^3H ("1") and ^{14}C ("2") from the following equations:

$$c_1 = [(y_1 - b_1) - a_{12}(y_2 - b_2)] / (1 - a_{12} a_{21}) V$$

$$c_2 = [(y_2 - b_2) - a_{21}(y_1 - b_1)] / (1 - a_{12} a_{21}) V$$

where V is the volume of the test sample.

- (4) Calculate water permeability for an interval from t_1 to t_2 as follows:

$$P = V_H [c_H(t_2) - c_H(t_1)] / A(c_I - c_H)(t_1 - t_2)$$

where V_H is the volume of Chamber II, $c_H(t_2)$ is the concentration of ^3H in Chamber II at time t_2 , $c_H(t_1)$ is the concentration of ^3H in Chamber II at time t_1 , A is the area of lens exposure, c_I is the average concentration of ^3H in Chamber I over the time period t_1 to t_2 and c_H is the average concentration of ^3H in Chamber II over the time period t_1 to t_2 .

The ophthalmic lenses of one embodiment of the present invention have a Hydrodell Water Permeability Coefficient of greater than about $0.2 \times 10^{-6} \text{ cm}^2/\text{min}$. The ophthalmic lenses in a preferred embodiment of the invention have Hydrodell Water Permeability Coefficient of greater than about $0.3 \times 10^{-6} \text{ cm}^2/\text{min}$. The ophthalmic lenses in a preferred embodiment of the invention have Hydrodell Water Permeability Coefficient of greater than about $0.4 \times 10^{-6} \text{ cm}^2/\text{min}$.

G. Oxygen Transmissibility and Permeability

As mentioned earlier, the cornea receives oxygen primarily from the corneal surface which is exposed to the environment, in contrast to other tissues which receives oxygen from blood flow. Thus, an ophthalmic lens which may be worn on the eye for extended periods of time must allow sufficient oxygen to permeate through the lens to the cornea to sustain corneal health. One result of the cornea receiving an inadequate amount of oxygen is that the cornea will swell. In a preferred embodiment, the oxygen transmissibility of the present ophthalmic lenses is sufficient to prevent any clinically significant amount of corneal swelling from occurring.

A preferred ophthalmic lens material will have an oxygen transmissibility, Dk/t , of at least $70 (\text{cm}^3 \text{ oxygen})(\text{mm})/\text{mm} \cdot \text{cm}^2 \cdot 33 (\text{sec}/\text{mm Hg}) \times 10^{-9}$ or [barrers/mm], more preferably at least 75 barrers/mm, and most preferably at least 87 barrers/mm.

The oxygen permeability of a lens and oxygen transmissibility of a lens material may be determined by the following technique. Oxygen fluxes (J) are measured at 34 C. in a wet cell (i.e., gas streams are maintained at about 100% relative humidity) using a Dk1000 instrument (available from Applied Design and Development Co., Norcross, Ga.), or similar analytical instrument. An air stream, having a known percentage of oxygen (e.g., 21%), is passed across one side of the lens at a rate of about 10 to 20 cm^3/min , while a nitrogen stream is passed on the opposite side of the lens at a rate of about 10 to 20 cm^3/min . The barometric pressure surrounding the system, P_{measured} , is measured. The thickness (t) of the lens in the area being exposed for testing is determined by measuring about 10 locations with a Mitotoya micrometer VL-50, or similar instrument, and averaging the measurements. The oxygen concentration in the nitrogen stream (i.e., oxygen which diffuses through the lens) is measured using the DK1000 instrument. The oxygen

16

permeability of the lens material, D_k , is determined from the following formula:

$$D_k = Jt / (P_{\text{oxygen}})$$

5 where

J=oxygen flux [microliters $\text{O}_2/\text{cm}^2 \cdot \text{minute}$]

$P_{\text{oxygen}} = (P_{\text{measured}} - P_{\text{water vapor}}) \times (\% \text{O}_2 \text{ in air stream})$ [mm Hg]=partial pressure of oxygen in the air stream

P_{measured} =barometric pressure [mm Hg]

$P_{\text{water vapor}}$ =0 mm Hg at 34 C. (in a dry cell) [mm Hg]

$P_{\text{water vapor}}$ =40 mm Hg at 34 C. (in a wet cell) [mm Hg]

t=average thickness of the lens over the exposed test area [mm]

where D_k is expressed in units of barrers, i.e., $[(\text{cc oxygen})(\text{mm})/\text{cm}^2] \times [\text{sec}/\text{mm Hg}] \times 10^{-10}$.

The oxygen transmissibility (D_k/t) of the material may be calculated by dividing the oxygen permeability (D_k) by the average thickness (t) of the lens.

H. Mechanical On-eye Movement Parameters

On-eye movement of a lens may be predicted from the mechanical properties of a lens, the ion or water permeability through the lens, or both the mechanical properties and ion or water permeability. In fact, on-eye movement may be predicted more accurately from a combination of mechanical properties and ion or water permeability.

1. Tensile Modulus and Short Relaxation Time

Tensile mechanical testing may be performed on lens materials to determine mechanical properties. A procedure for preparing a test sample from a lens for subsequent mechanical testing includes the following steps:

1. Cut a parallel-sided strip through the center of the lens. A suitable width for the strip is about 3.1 mm.

2. Immerse the test strip in a phosphate-buffered saline solution (approximating ocular fluid osmolality) for a period of about 24 hours before testing.

3. Conduct mechanical testing with the test strip immersed in phosphate-buffered saline at ambient temperature (about 23° C.).

Tensile modulus may be measured by applying a strain rate of about 100% per minute to the test strip and recording the resultant stress. However, the procedure may be used at differing strain rates.

Stress relaxation is measured by applying a constant strain of about 5% to the test strip and recording the resultant stress for about 5 minutes. A useful mechanical testing instrument for this type of testing is the Vitrodyne V-200 from Liveco Biomechanical Instruments, located in Burlington, Vt.

In order to analyze stress relaxation data, a three element Maxwell-Wiechert model (a spring and two spring-dashpot elements in parallel) may be assumed for the polymer material. For this model the stress relaxation modulus is given by the following equation:

$$E(t) = E_0 + E_1 \exp(-t/t_1) + E_2 \exp(-t/t_2)$$

Stress v. time curves may be normalized to the maximum (initial) stress induced in the samples. These curves may be analyzed by a variety of commercially available software (for example, ORIGIN software) by fitting the double exponential equation:

$$y(t) = y_0 + A_1 \exp(-t/t_1) + A_2 \exp(-t/t_2)$$

in order to obtain the stress relaxation parameters y_0 , t_1 , A_1 , t_2 , and A_2 .

It has been determined that the tensile modulus (modulus of elasticity, E) and the short relaxation time constant (t_1)

US 6,951,894 B1

17

correlate well with on-eye movement. In order to have appropriate on-eye movement, a lens preferably has a tensile modulus of less than about 3 MPa. More preferably, E is about 0.4 to about 2.5 MPa while a particularly preferred E is about 0.5 to about 1.5 MPa.

A preferred short relaxation time constant (t_1) is greater than about 3.5 seconds. More preferably, t_1 is greater than about 4 seconds, while a particularly preferred t_1 is greater than about 4.5 seconds.

2. Tangent Delta

Lenses may also be evaluated by dynamic mechanical analysis (DMA) methods. It has been determined that a factor known as $\tan \delta$ (i.e., tangent delta), also known as mechanical loss factor, correlates well with on-eye movement. It has been observed that lens materials which move on the eye exhibit a distinct increase in $\tan \delta$ with increasing frequency from about 0.1 to 10 Hz when these materials are tested by dynamic mechanical analysis. The $\tan \delta$ of a preferred lens material is above about 0.2 at 0.1 Hz and increases to about 0.25 or more at about 10 Hz. A $\tan \delta$ of about 0.3 or greater at 10 Hz is more preferred, while a $\tan \delta$ of about 0.5 or greater at 10 Hz is even more preferred.

DMA measurements may be determined in accordance with the following procedure. A disk of lens material having a diameter of about 3.0 mm and a thickness of about 0.50 mm is formed. The disk is placed in a Perkin-Elmer DMA-7 instrument. The disk is immersed in a solution buffered to a pH of about 7.2 and held isothermally for a period of about 10 minutes or more prior to testing, at a temperature of about 23 to 35° C. The instrument is set to a compression measuring mode and the strain on the sample is adjusted to about 2% to 4%, depending on the sample response. The amplitude of compression is about 2 to 4 μ m. Measurements of the modulus of elasticity and $\tan \delta$ are taken at frequencies of about 0.1, about 1, and about 10 Hz.

3. Parameter Combinations

In order to assure appropriate movement of the lens on the eye, one may select materials which have a combination of the above-discussed properties. Therefore, a preferred group of extended-wear contact lens materials have (a) a modulus of elasticity (E) of about 1.5 MPa or less, (b) a short time relaxation constant (t_1) of greater than about 4 seconds, and (c) an Ionoton Ion Permeability Coefficient of greater than about 0.3×10^{-6} cm²/sec and/or an Ionoflux Diffusion Coefficient greater than about 6.4×10^{-6} mm²/min.

I. Examples of Suitable Materials

1. Material "A"

One embodiment of a suitable core material of the present ophthalmic lenses is a copolymer formed from the following monomeric and macromeric components:

- (a) about 5 to about 94 dry weight percent of a macromer having the segment of the formula



where

PDMS is a divalent poly(disubstituted siloxane),

ALK is an alkylene or alkylenoxy group having at least 3 carbon atoms,

DU is a diurethane-containing group,

PAO is a divalent polyoxyalkylene, and

CP is selected from acrylates and methacrylates, wherein said macromer has a number-average molecular weight of 2000 to 10,000;

- (b) about 5 to about 60 weight percent methacryloxypropyltris(trimethylsiloxy)silane;

18

- (c) about 1 to about 30 weight percent of an acrylate or methacrylate monomer; and

- (d) 0 to 5 weight percent cross-linking agent, with the weight percentages being based upon the dry weight of the polymer components.

A preferred polysiloxane macromer segment is defined by the formula



where

PDMS is a divalent poly(disubstituted siloxane);

CP is an isocyanatoalkyl acrylate or methacrylate, preferably isocyanatoethyl methacrylate, where the urethane group is bonded to the terminal carbon on the PAO group;

PAO is a divalent polyoxyalkylene (which may be substituted), and is preferably a polyethylene oxide, i.e., $(-\text{CH}_2-\text{CH}_2-\text{O}-)_m\text{CH}_2\text{CH}_2-$ where m may range from about 3 to about 44, more preferably about 4 to about 24;

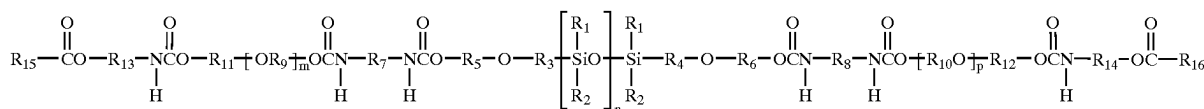
DU is a diurethane, preferably including a cyclic structure, where an oxygen of the urethane linkage (1) is bonded to the PAO group and an oxygen of the urethane linkage (2) is bonded to the ALK group;

and ALK is an alkylene or alkylenoxy group having at least 3 carbon atoms, preferably a branched alkylene group or an alkylenoxy group having 3 to 6 carbon atoms, and most preferably a sec-butyl (i.e., $-\text{CH}_2\text{CH}_2\text{CH}(\text{CH}_3)-$) group or an ethoxypropoxy group (e.g., $-\text{O}-(\text{CH}_2)_2-\text{O}-(\text{CH}_2)_3-$).

It will be noted that the DU group can be formed from a wide variety of diisocyanates or triisocyanates, including aliphatic, cycloaliphatic or aromatic polyisocyanates. These isocyanates include, without limitation thereto, ethylene diisocyanate; 1,2-diisocyanatopropane; 1,3-diisocyanatopropane; 1,6-diisocyanatohexane; 1,2-diisocyanatocyclohexane; 1,3-diisocyanatocyclohexane; 1,4-diisocyanatobenzene, bis(4-isocyanatocyclohexyl)methane; bis(4-isocyanatocyclohexyl)methane, bis(4-isocyanatophenyl)methane; 1,2- and 1,4-toluene diisocyanate; 3,3'-dichloro-4,4'-diisocyanatobiphenyl; tris(4-isocyanatophenyl)methane; 1,5-diisocyanatonaphthalene; hydrogenated toluene diisocyanate; 1-isocyanatomethyl-5-isocyanato-1,3,3-trimethylcyclohexane (i.e., isophorone diisocyanate); 1,3,5-tris(6-isocyanatoethyl) biuret; 1,6-diisocyanato-2,2,4-(2,4,4)-trimethylhexane; 2,2'-diisocyanatodiethyl fumarate; 1,5-diisocyanato-1-carboxypentane; 1,2-, 1,3-, 1,6-, 1,7-, 1,8-, 2,7- and 2,3-diisocyanatonaphthalene; 2,4- and 2,7-diisocyanato-1-methylnaphthalene; 1,4-diisocyanatomethylcyclohexane; 1,3-diisocyanato-6(7)-methylnaphthalene; 4,4'-diisocyanatobiphenyl; 4,4'-diisocyanato-3,3'-dimethoxybisphenyl; 3,3'- and 4,4'-diisocyanato-2,2'-dimethylbisphenyl; bis(4-isocyanatophenyl) ethane; bis(4-isocyanatophenyl ether); 1,2- or 1,4-toluene diisocyanate; and mixtures thereof. Preferably DU is formed from isophorone diisocyanate or toluene diisocyanate, and more preferably, isophorone diisocyanate, where one isomeric diurethane structure of isophorone diisocyanate is defined above.

19

A preferred Material A macromer segment has the following formula:



wherein:

R₁ and R₂ are lower alkyl (C₁-C₆), preferably C₁-C₃ alkyl, more preferably methyl;

R₃, R₄, R₅, and R₆ are lower alkylene (C₁–C₆), preferably C₁–C₃ alkylene, more preferably C₂–C₃ alkylene, and preferably, where the total number of carbon atoms in R₃ and R₅, or R₄ and R₆ is greater than 4;

R₇ and R₈ are linear or branched alkylene or an bivalent cycloalkylene, preferably bivalent cycloalkylene;

R₉, R₁₀, R₁₁, and R₁₂ are C₁-C₂ alkylene, preferably C₂ alkylene;

R₁₃ and R₁₄ are lower alkenylene (C₁-C₆), preferably C₁-C₃ alkenylene, more preferably ethylene; and

R₁₅ and R₁₆ are linear or branched lower alkenylene, preferably C₂-C₃ alkenylene;

m and p, independently of one another, may range from about 3 to about 44, more preferably about 4 to about 24; and

n may range from about 13 to about 80, more preferably, about 20 to about 50, and even more preferably about 24 to about 30.

The polysiloxane macromer may be synthesized by the following preferred process. At about room temperature (about 20–25° C.), poly(dimethylsiloxane) dialkanol having hydroxyalkyl (e.g., hydroxy-sec-butyl) or hydroxyalkoxy (e.g., hydroxyethylpropoxy) end groups and having a molecular weight of about 2000 to 3000 (preferably about 2200, i.e., having about 28 repeating siloxane groups) is reacted with isophorone diisocyanate at about a 1:2 molar ratio, using about 0.2 weight percent (based on polydimethylsilane) dibutyltin dilaurate added as a catalyst. The reaction is carried out for about 36 to 60 hours. To this mixture is added poly(ethylene glycol) having a molecular weight of about 400 to 1200 (more preferably about 500 to 700) at about a 2:1 or 2.1:1 molar ratio with respect to the PDMS, about 0.4 to 0.5 weight percent dibutyltin dilaurate (based on polyethylene glycol weight), and chloroform sufficient to ensure substantial mixture homogeneity. The mixture is agitated for about 12 to 18 hours, then held at a temperature of about 44 to 48° C. for about 6 to 10 hours. Excess chloroform is evaporated therefrom at about room temperature to produce a composition having about 50 weight percent solids. Then, isocyanatoethyl methacrylate is added to the mixture in about a 2:1 to 2.3:1 molar ratio with respect to PDMS. The mixture is agitated at room temperature for about 15 to 20 hours. The resulting solution contains a polysiloxane macromer having the composition described above and a number-average molecular weight of about 2000 to 10,000, more preferably about 3000 to 5000.

An advantageous polymeric material formed from the Material A macromer of the present invention is a copolymer of the aforementioned Material A macromer; an acrylated or methacrylated siloxane monomer, preferably methacryloxypopyltris (trimethylsiloxy) silane (referred to herein as "Tris"); a hydrophilic monomer, preferably 2-hydroxyethyl

20

methacrylate (HEMA); and preferably, a cross-linking agent such as ethylene glycol dimethacrylate (EGDMA). The final

copolymer composition includes about 10 to 90, preferably 70 to 90, weight percent polysiloxane macromer; about 5 to 60, preferably about 8 to 20, weight percent siloxane monomer; about 1 to 30, preferably about 1 to 5, weight percent acrylate or methacrylate monomer; and 0 to about 5, preferably up to about 2 weight percent cross-linking agent (e.g., EGDMA) based on a total dry copolymer weight. A more preferred composition includes about 80 to 84 polysiloxane macromer, about 12 to 15 weight percent TRIS, about 3 to about 4 weight percent 2-hydroxyethyl methacrylate, and about 0.7 to about 1.2 weight percent ethylene glycol dimethacrylate.

The advantageous copolymers of the present invention may be formed from the previously-described polysiloxane macromer in the following manner. A monomeric solution is formed by adding Tris, HEMA, DAROCUR® 1173 (a photoinitiator available from Ciba-Geigy Corporation), and optionally, EGDMA to the polysiloxane macromer solution. The resulting polymer precursor solution preferably contains about 83 to about 95 weight percent polysiloxane macromer solution, about 5 to about 10 weight percent Tris, about 0.5 to about 5 weight percent HEMA, about 0.1 to about 1.0 weight percent DAROCUR® 1173, and about 0.1 to about 1.0 weight percent EGDMA. More preferably, the monomer solution contains about 87 to about 93 weight percent polysiloxane macromer solution, about 7 to about 8 weight percent Tris, about 2 to about 4 weight percent HEMA, about 0.3 to about 0.7 weight percent DAROCUR® 1173, and about 0.3 to about 0.7 weight percent EGDMA. The monomer solution is preferably agitated for about 8 to about 24 hours prior to the polymerization step.

Contact lenses may be prepared from the monomer solution by applying the monomer solution to appropriate lens molds and applying sufficient ultraviolet (UV) radiation to initiate polymerization. The ultraviolet light may be applied for a period of a few minutes to about 5 hours, depending on the intensity of light applied. Subsequent to polymerization, the contact lens may be extracted with a solvent, e.g., isopropanol, to remove unreacted monomers.

Thus, generally, one embodiment of the present invention is a method of forming a molded polymeric article suitable for ophthalmic applications (especially a contact lens), including the following steps:

- (a) contacting a poly(dialkylsiloxane) dialkanol with a diisocyanate compound in the presence of a first catalyst at conditions sufficient to cause reaction of said dialkanol with said diisocyanate, thereby forming a first mixture;
- (b) contacting said first mixture with poly(alkylene glycol), a second catalyst, and sufficient solvent to ensure mixture homogeneity, thereby forming a second mixture;
- (c) evaporating sufficient solvent from said second mixture to generate a third mixture having a solids content of about 40 to 60 weight percent;
- (d) adding isocyanatoalkyl methacrylate to said third mixture, thereby forming a fourth mixture containing a polysiloxane macromer;

US 6,951,894 B1

21

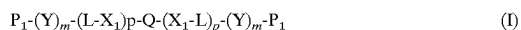
- (e) adding to said fourth mixture 3-methacryloxypropyltris(trimethylsiloxy)silane (TRIS), a hydrophilic monomer, a cross-linking agent and a photoinitiator, thereby forming a fifth mixture;
- (f) placing said fifth mixture into a mold; and
- (g) applying sufficient radiation to copolymerize said monomers, thereby forming said polymeric material into a molded polymeric article.

The hydrophilic copolymers of the present invention are especially advantageous in the formation of "soft" contact lenses. In the use of the copolymers in the contact lens field, the lenses have a water content of about 10 to about 50 weight percent, more preferably about 10 to about 30 weight percent, and most preferably about 15 to about 22 weight percent, based on total hydrophilic polymer weight. Preferably, the fully-hydrated contact lens has an oxygen transmissibility (D_k/t) of greater than 70 barrers/mm (i.e., $[(\text{cc oxygen})(\text{mm})/\text{cm}^2] \times [\text{sec}/\text{mm Hg}] \times 10^{-10}$), more preferably greater than about 75 barrers/mm, and most preferably greater than about 87 barrers/mm.

2. Material "B"

Polysiloxane-comprising perfluoroalkyl ethers

The Material "B" macromer is defined by formula (I):



where

each P_1 , independently of the others, is a free-radical-polymerizable group;

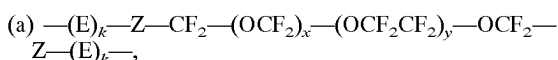
each Y , independently of the others, is $-\text{CONHCOO}-$, $-\text{CONHCONH}-$, $-\text{OCONHCO}-$, $-\text{NHCONHCO}-$, $-\text{NHCO}-$, $-\text{CONH}-$, $-\text{NHCONH}-$, $-\text{COO}-$, $-\text{OCO}-$, $-\text{NHCOO}-$ or $-\text{OCONH}-$;

m and p , independently of one another, are 0 or 1;

each L , independently of the others, is a divalent radical of an organic compound having up to 20 carbon atoms;

each X_1 , independently of the others, is $-\text{NHCO}-$, $-\text{CONH}-$, $-\text{NHCONH}-$, $-\text{COO}-$, $-\text{OCO}-$, $-\text{NHCOO}-$ or $-\text{OCONH}-$; and

Q is a bivalent polymer fragment consisting of the segments:



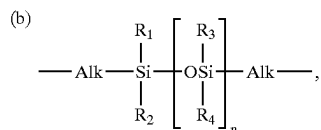
where

$x+y$ is a number in the range of 10 to 30;

each Z , independently of the others, is a divalent radical having up to 12 carbon atoms or Z is a bond;

each E , independently of the others, is $-(\text{OCH}_2\text{CH}_2)_q-$, where q has a value of from 0 to 2, and where the link ---Z---E--- represents the sequence $\text{---Z---}(\text{OCH}_2\text{CH}_2)_q\text{---}$; and

k is 0 or 1;



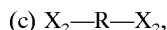
where

n is an integer from 5 to 100;

Alk is alkylene having up to 20 carbon atoms;

80–100% of the radicals R_1 , R_2 , R_3 and R_4 , independently of one another, are alkyl and 0–20% of the radicals R_1 , R_2 , R_3 and R_4 , independently of one another, are alkenyl, aryl or cyanoalkyl; and

22



where

R is a divalent organic radical having up to 20 carbon atoms, and

each X_2 , independently of the others, is $-\text{NHCO}-$, $-\text{CONH}-$, $-\text{NHCONH}-$, $-\text{COO}-$, $-\text{OCO}-$, $-\text{NHCOO}-$ or $-\text{OCONH}-$;

with the provisos that there must be at least one of each segment (a), (b), and (c) in Q , that each segment (a) or (b) has a segment (c) attached to it, and that each segment (c) has a segment (a) or (b) attached to it.

The number of segments (b) in the polymer fragment Q is preferably greater than or equal to the number of segments (a). The ratio between the number of segments (a) and (b) in the polymer fragment Q is preferably 3:4, 2:3, 1:2 or 1:1. The molar ratio between the number of segments (a) and (b) in the polymer fragment Q is more preferably 2:3, 1:2 or 1:1.

The mean molecular weight of the polymer fragment Q is in the range of about 1000 to about 20000, preferably in the range of about 3000 to about 15000, particularly preferably in the range of about 5000 to about 12000.

The total number of segments (a) and (b) in the polymer fragment Q is preferably in the range of 2 to about 11, particularly preferably in the range of 2 to about 9, and in particular in the range of 2 to about 7. The smallest polymer unit Q is preferably composed of one perfluoro segment (a), one siloxane segment (b) and one segment (c).

In a preferred embodiment of the polymer fragment Q , which preferably has a composition in the abovementioned ratios, the polymer fragment Q is terminated at each end by a siloxane segment (b).

The compositions in a bivalent polymer fragment Q always correspond above and below to a mean statistical composition. This means that, for example, even individual block copolymer radicals containing identical recurring units are included, so long as the final mean statistical composition is as specified.

X_1 is preferably $-\text{NHCONH}-$, $-\text{NHCOO}-$ or $-\text{OCONH}-$, particularly preferably $-\text{NHCOO}-$ or $-\text{OCONH}-$.

The $X_2\text{---R---X}_2$ segment is preferably a radical derived from a diisocyanate, where each X_2 , independently of the other, is $\text{NHCONH}-$, $\text{NHCOO}-$ or $\text{OCONH}-$, in particular $\text{NHCOO}-$ or $\text{OCONH}-$.

Z is preferably a bond, lower alkylene or $-\text{CONH}-$ arylene, in which the $-\text{CO}-$ moiety is linked to a CF_2 group. Z is particularly preferably lower alkylene, in particular methylene.

q is preferably 0, 1, 1.5 or 2, particularly preferably 0 or 1.5.

The perfluoroalkoxy units OCF_2 and OCF_2CF_2 with the indices x and y in segment (a) can either have a random distribution or be in the form of blocks in a chain. The sum of the indices $x+y$ is preferably a number in the range of 10 to 25, particularly preferably of 10 to 15. The ratio $x:y$ is preferably in the range of 0.5 to 1.5, in particular in the range of 0.7 to 1.1.

A free-radical-polymerizable group P_1 is, for example, alkenyl, alkenylaryl or alkenylarylenealkyl having up to 20 carbon atoms. Examples of alkenyl are vinyl, allyl, 1-propen-2-yl, 1-buten-2-, -3- and -4-yl, 2-buten-3-yl, and the isomers of pentenyl, hexenyl, octenyl, decenyl and undecenyl. Examples of alkenylaryl are vinylphenyl, vinyl-naphthyl or allylphenyl. An example of alkenylarylenealkyl is *o*-, *m*-, or *p*-vinylbenzyl.

P_1 is preferably alkenyl or alkenylaryl having up to 12 carbon atoms, particularly preferably alkenyl having up to 8 carbon atoms, in particular alkenyl having up to 4 carbon atoms.

US 6,951,894 B1

23

Y is preferably —COO—, —OCO—, —NHCONH—, —NHCOO—, —OCONH—, NHCO— or —CONH—, particularly preferably —COO—, —OCO—, NHCO— or —CONH—, and in particular, —COO— or —OCO—.

In a preferred embodiment, the indices, m and p, are not simultaneously zero. If p is zero, m is preferably 1.

L is preferably alkylene, arylene, a saturated bivalent cycloaliphatic group having 6 to 20 carbon atoms, arylenealkylene, alkylenearylene, alkylenearylenealkylene or arylenealkylenearylene.

Preferably, L is a divalent radical having up to 12 carbon atoms, particularly preferably a divalent radical having up to 8 carbon atoms. In a preferred embodiment, L is furthermore alkylene or arylene having up to 12 carbon atoms. A particularly preferred embodiment of L is lower alkylene, in particular lower alkylene having up to 4 carbon atoms.

The divalent radical R is, for example, alkylene, arylene, alkylenearylene, arylenealkylene or arylenealkylenearylene having up to 20 carbon atoms, a saturated bivalent cycloaliphatic group having 6 to 20 carbon atoms or cycloalkylenealkylenecycloalkylene having 7 to 20 carbon atoms.

In a preferred embodiment, R is alkylene, arylene, alkylenearylene, arylenealkylene or arylenealkylenearylene having up to 14 carbon atoms or a saturated divalent cycloaliphatic group having 6 to 14 carbon atoms. In a particularly preferred embodiment, R is alkylene or arylene having up to 12 carbon atoms or a saturated bivalent cycloaliphatic group having 6 to 14 carbon atoms.

In a preferred embodiment, R is alkylene or arylene having up to 10 carbon atoms or a saturated bivalent cycloaliphatic group having 6 to 10 carbon atoms.

In a particularly preferred meaning, R is a radical derived from a diisocyanate, for example from hexane 1,6-diisocyanate, 2,2,4-trimethylhexane 1,6-diisocyanate, tetramethylene diisocyanate, phenylene 1,4-diisocyanate, toluene 2,4-diisocyanate, toluene 2,6-diisocyanate, m- or p-tetramethylxylene diisocyanate, isophorone diisocyanate or cyclohexane 1,4-diisocyanate.

In a preferred meaning, n is an integer from 5 to 70, particularly preferably 10 to 50, in particular 14 to 28.

In a preferred meaning, 80–100%, preferably 85–100%, in particular 90–100%, of the radicals R₁, R₂, R₃ and R₄ are, independently of one another, lower alkyl having up to 8 carbon atoms, particularly preferably lower alkyl having up to 4 carbon atoms, especially lower alkyl having up to 2 carbon atoms. A further particularly preferred embodiment of R₁, R₂, R₃ and R₄ is methyl.

In a preferred meaning, 0–20%, preferably 0–15%, in particular 0–10%, of the radicals R₁, R₂, R₃ and R₄ are, independently of one another, lower alkenyl, unsubstituted or lower alkyl- or lower alkoxy-substituted phenyl or cyano (lower alkyl).

Arylene is preferably phenylene or naphthylene, which is unsubstituted or substituted by lower alkyl or lower alkoxy, in particular 1,3-phenylene, 1,4-phenylene or methyl-1,4-phenylene, 1,5-naphthylene or 1,8-naphthylene.

Aryl is a carbocyclic aromatic radical which is unsubstituted or substituted preferably by lower alkyl or lower alkoxy. Examples are phenyl, tolyl, xylyl, methoxyphenyl, t-butoxyphenyl, naphthyl and phenanthryl.

A saturated bivalent cycloaliphatic group is preferably cycloalkylene, for example cyclohexylene or cyclohexylene (lower alkylene), for example cyclohexylenemethylene, which is unsubstituted or substituted by one or more lower alkyl groups, for example methyl groups, for example trimethylcyclohexylenemethylene, for example the bivalent isophorone radical.

24

For the purposes of the present invention, the term “lower” in connection with radicals and compounds, unless defined otherwise, denotes, in particular, radicals or compounds having up to 8 carbon atoms, preferably having up to 4 carbon atoms.

Lower alkyl has, in particular, up to 8 carbon atoms, preferably up to 4 carbon atoms, and is, for example, methyl, ethyl, propyl, butyl, tert-butyl, pentyl, hexyl or isohexyl.

Alkylene has up to 12 carbon atoms and can be straight-chain or branched. Suitable examples are decylene, octylene, hexylene, pentylene, butylene, propylene, ethylene, methylene, 2-propylene, 2-butylene, 3-pentylene, and the like.

Lower alkylene is alkylene having up to 8 carbon atoms, particularly preferably up to 4 carbon atoms. Particularly preferred meanings of lower alkylene are propylene, ethylene and methylene.

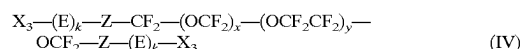
The arylene unit in alkylenearylene or arylenealkylene is preferably phenylene, unsubstituted or substituted by lower alkyl or lower alkoxy, and the alkylene unit therein is preferably lower alkylene, such as methylene or ethylene, in particular methylene. These radicals are therefore preferably phenylenemethylene or methylenephenylene.

Lower alkoxy has, in particular, up to 8 carbon atoms, preferably up to 4 carbon atoms, and is, for example, methoxy, ethoxy, propoxy, butoxy, tert-butoxy or hexyloxy.

Arylenealkylenearylene is preferably phenylene(lower alkylene)phenylene having up to 8, in particular up to 4, carbon atoms in the alkylene unit, for example phenylene-ethylenephenylene or phenylenemethylenephenylene.

The macromers of the formula (I) can be prepared by processes known per se, for example as follows:

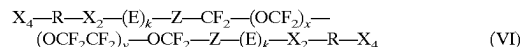
In a first step, a perfluoropolyalkyl ether derivative of formula (IV):



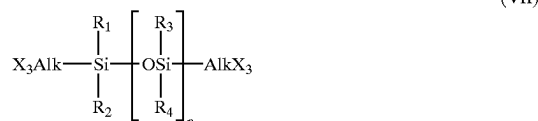
in which X₃ is —OH, —NH₂, —COOH, —COCl, —NCO or —COOR₅, where —COOR₅ is generally an activated ester in which R₅ is alkyl or aryl which is unsubstituted or substituted by halogen or cyano, and the variables Z, E, k, x and y are as defined above, is preferably reacted with two equivalents of a bifunctional radical of formula (V):



in which R is as defined above and X₄ is a functional radical which is coreactive with an X₃ and is preferably —OH—, —NH₂, COOH, —COCl, —COOR₅ or —NCO; in the presence or absence of a suitable catalyst, where the reaction of X₃ with X₄ gives a group X₂; after which a reactive derivative of formula (VI):



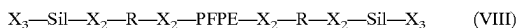
is obtained which is then preferably reacted with two equivalents of an α,ω-substituted siloxane of formula (VII):



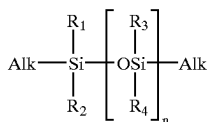
where the variables R₁, R₂, R₃, R₄, n, X₃ and Alk are as defined above, in the presence or absence of a suitable catalyst, giving a compound of formula (VIII):

US 6,951,894 B1

25



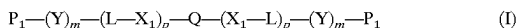
in which PFPE is $(E)_k-Z-CF_2-(OCF_2)_x-(OCF_2CF_2)_y-CF_2-Z-(E)_k$, Sil is the siloxane radical



and the other variables are as defined above; after which the reactive intermediate of the formula (VIII) is preferably reacted with two equivalents of a compound of the formula (IXa) or (IXb):



in the presence or absence of a catalyst, to give the macromer of the formula (I):



in which Y_2 is a functional radical which is coreactive with X_3 and is preferably $-OH$, $-NH_2$, $-COOH$, $-COCl$, $-COOR_5$, $-CONCO$ or $-NCO$, and the variables are as defined above, and in which X_4 is formed from the reaction of X_3 with X_4 and Y is formed from the reaction of Y_2 with X_3 .

The starting materials of formula (IV) for the preparation of the perfluoroalkyl ethers are known and many are commercially available. For example, U.S. Pat. No. 3,810,875 and European Patent No. 0211237 (U.S. Pat. No. 4,746,575) describe such compounds. Ausimont, Italy, markets perfluoroalkyl ether dimethanols under the name Fomblin, for example Fomblin ZDOL and Fomblin ZDOL-TX. Further Fomblin derivatives of the formula (IV) are commercially available, including, for example, Fomblin ZDISOC, in which the radical $-Z-X_3$ in the formula (IV) is $CONH-C_6H_3(CH_3)-NCO$; Fomblin ZDEAL, in which the radical $-Z-X_3$ in the formula (IV) is $-COOR_5$; and Fomblin ZDIAC, in which the radical $-Z-X_3$ in the formula (IV) is $-COOH$.

Bifunctional radicals having a substitution pattern as per formula (V) exist in large numbers and are commercially available. Examples include, without limitation thereto: diisocyanates, such as isophorone diisocyanate and 2,2,4-trimethylhexane 1,6-diisocyanate; diols, such as glycol and cyclohexane-1,2-diol; dicarboxylic acids, such as adipic acid and maleic acid; diamines, such as ethylenediamine and hexamethylenediamine, diesters, such as diethyl phthalate and dibutyl malonate; derivatives containing various functional groups, such as 2-aminoethanol, monomethyl malonate, glycolic acid, salicylic acid, glycine and glycine methyl ester.

Preference is given to bifunctional derivatives of the formula (V) which have different reactivities irrespective of the nature of their functional radicals X_4 . In the case of identical radicals X_4 , this is achieved, for example, through different steric requirements in the direct vicinity of a radical X_4 . Examples thereof are isophorone diisocyanate, 2,2,4-trimethylhexane 1,6-diisocyanate and toluene 2,4-diisocyanate. The advantage of using bifunctional derivatives of formula (V) of different reactivity is that the chain length of polymer Q (number of segments (a), (b) and (c)) is easily adjustable and controllable.

α,ω -substituted siloxanes of formula (VII) are likewise commercially available, for example α,ω -hydroxypropyl-terminated polydimethylsiloxane KF6001 from Shin-Etsu.

26

The novel compounds can be prepared in the presence or absence of a solvent. It is advantageous to use a substantially inert solvent, i.e., one which does not participate in the reaction. Suitable examples thereof are ethers, such as tetrahydrofuran (THF), diethyl ether, diethylene glycol dimethyl ether or dioxane, halogenated hydrocarbons, such as chloroform or methylene chloride, bipolar aprotic solvents, such as acetonitrile, acetone, dimethylformamide (DMF) or dimethyl sulfoxide (DMSO), hydrocarbons, such as hexane, petroleum ether, toluene or xylene, and furthermore pyridine or N-methylmorpholine.

In the preparation of novel compounds, the reactants are advantageously employed in stoichiometric amounts. The reaction temperature can be, for example, from -30°C . to 150°C ., preferably from 0° to room temperature. The reaction times are in the range of about 15 minutes to 7 days, preferably about 12 hours. If necessary, the reaction is carried out under argon or nitrogen as protective gas. In urethane-forming reactions, a suitable catalyst, for example, dibutyltin dilaurate (DBTDL), is advantageously added.

The present Material "B" furthermore relates to a polymer comprising a product of the polymerization of at least one compound of formula (I) as defined above and, if desired, at least one vinylic comonomer (a). In a preferred composition of a novel copolymer, the proportion by weight of a compound of formula (I) is in the range of 100 to 0.5%, in particular in the range of 80 to 10%, preferably in the range of 70 to 30%, based on the total polymer.

In a preferred polymer comprising a product of the polymerization of at least one compound of the formula (I), comonomer (a) is absent and the polymer is a homopolymer.

A comonomer (a) present in the novel polymer can be hydrophilic or hydrophobic or a mixture thereof. Suitable comonomers are, in particular, those which are usually used in the production of contact lenses and biomedical materials. A hydrophobic comonomer (a) is taken to mean a monomer which typically gives a homopolymer which is insoluble in water and can absorb less than 10% by weight of water. Analogously, a hydrophilic comonomer (a) is taken to mean a monomer which typically gives a homopolymer which is soluble in water or can absorb at least 10% by weight of water. Suitable hydrophobic comonomers (a) are, without limitation thereto, C_1-C_{18} alkyl and C_3-C_{18} cycloalkyl acrylates and methacrylates, C_3-C_{18} alkylacrylamides and -methacrylamides, acrylonitrile, methacrylonitrile, vinyl C_1-C_{18} alkanoates, C_2-C_{18} alkenes, C_2-C_{18} haloalkenes, styrene, (lower alkyl)styrene, lower alkyl vinyl ethers, C_2-C_{10} perfluoroalkyl acrylates and methacrylates and correspondingly partially fluorinated acrylates and methacrylates,

C_3-C_{12} perfluoroalkylethylthiocarbonylaminoethyl acrylates and methacrylates, acryloxy- and methacryloxyalkylsiloxanes, N-vinylcarbazole, C_1-C_{12} alkyl esters of maleic acid, fumaric acid, itaconic acid, mesaconic acid and the like.

Preference is given, for example, to acrylonitrile, C_1-C_4 alkyl esters of vinylically unsaturated carboxylic acids having 3 to 5 carbon atoms or vinyl esters of carboxylic acids having up to 5 carbon atoms.

Examples of suitable hydrophobic comonomers (a) are methyl acrylate, ethyl acrylate, propyl acrylate, isopropyl acrylate, cyclohexyl acrylate, 2-ethylhexyl acrylate, methyl methacrylate, ethyl methacrylate, propyl methacrylate, butyl acrylate, vinyl acetate, vinyl propionate, vinyl butyrate, vinyl valerate, styrene, chloroprene, vinyl chloride, vinylidene chloride, acrylonitrile, 1-butene, butadiene, methacrylonitrile, vinyltoluene, vinyl ethyl ether, perfluoro-

US 6,951,894 B1

27

hexylethylthiocarbonylaminoethyl methacrylate, isobornyl methacrylate, trifluoroethyl methacrylate, hexafluoroisopropyl methacrylate, hexafluorobutyl methacrylate, tris(trimethylsilyloxy)silylpropyl methacrylate (TRIS), 3-methacryloxy propylpentamethyldisiloxane and bis(methacryloxypropyl) tetramethyldisiloxane.

Preferred examples of hydrophobic comonomers (a) are methyl methacrylate, TRIS and acrylonitrile.

Suitable hydrophilic comonomers (a) are, without this being an exhaustive list, hydroxyl-substituted lower alkyl acrylates and methacrylates, acrylamide, methacrylamide, (lower alkyl)acrylamides and -methacrylamides, ethoxylated acrylates and methacrylates, hydroxyl-substituted (lower alkyl)acrylamides and -methacrylamides, hydroxyl-substituted lower alkyl vinyl ethers, sodium vinylsulfonate, sodium styrenesulfonate, 2-acrylamido-2-methylpropanesulfonic acid, N-vinylpyrrole, N-vinyl-2-pyrrolidone, 2-vinylloxazoline, 2-vinyl-4,4'-dialkylloxazolin-5-one, 2- and 4-vinylpyridine, vinylically unsaturated carboxylic acids having a total of 3 to 5 carbon atoms, amino(lower alkyl)- (where the term "amino" also includes quaternary ammonium), mono(lower alkylamino)(lower alkyl) and di(lower alkylamino)(lower alkyl) acrylates and methacrylates, allyl alcohol and the like. Preference is given, for example, to N-vinyl-2-pyrrolidone, acrylamide, methacrylamide, hydroxyl-substituted lower alkyl acrylates and methacrylates, hydroxy-substituted (lower alkyl) acrylamides and -methacrylamides and vinylically unsaturated carboxylic acids having a total of 3 to 5 carbon atoms.

Examples of suitable hydrophilic comonomers (a) are hydroxyethyl methacrylate (HEMA), hydroxyethyl acrylate, hydroxypropyl acrylate, trimethylammonium 2-hydroxy propylmethacrylate hydrochloride (Blemer® QA, for example from Nippon Oil), dimethylaminoethyl methacrylate (DMAEMA), dimethylaminoethylmethacrylamide, acrylamide, methacrylamide, N,N-dimethylacrylamide (DMA), allyl alcohol, vinylpyridine, glycerol methacrylate, N-(1,1-dimethyl-3-oxobutyl)acrylamide, N-vinyl-2-pyrrolidone (NVP), acrylic acid, methacrylic acid and the like.

Preferred hydrophilic comonomers (a) are trimethylammonium 2-hydroxy propylmethacrylate hydrochloride, 2-hydroxyethyl methacrylate, dimethylaminoethyl methacrylate, trimethylammonium 2-hydroxypropylmethacrylate hydrochloride, N,N-dimethylacrylamide and N-vinyl-2-pyrrolidone.

The novel polymers are synthesized in a manner known per se from the corresponding monomers (the term monomer here also including a macromer according to the definition of the formula (I)) by a polymerization reaction customary to the person skilled in the art. Usually, a mixture of the abovementioned monomers is warmed with addition of a free-radical former. Examples of such free-radical formers are azoisobutyronitrile (AIBN), potassium peroxydisulfate, dibenzoyl peroxide, hydrogen peroxide and sodium percarbonate. If, for example, said compounds are warmed, free radicals form with homolysis, and can then initiate, for example, a polymerization.

A polymerization reaction can particularly preferably be carried out using a photoinitiator. In this case, the term photopolymerization is used. In the photopolymerization, it is appropriate to add a photoinitiator which can initiate free-radical polymerization and/or crosslinking by using light. Examples thereof are customary to the person skilled in the art; suitable photoinitiators are, in particular, benzoin methyl ether, 1-hydroxycyclohexylphenyl ketone, Darocur and Irgacur products, preferably Darocur® 1173 and Irga-

28

cur® 2959. Also suitable are reactive photoinitiators, which can be incorporated, for example, into a macromer, or can be used as a specific comonomer (a). Examples thereof are given in European Patent No. 0632329. The photopolymerization can then be initiated by actinic radiation, for example light, in particular UV light having a suitable wavelength. The spectral requirements can, if necessary, be controlled appropriately by addition of suitable photosensitizers.

A polymerization can be carried out in the presence or absence of a solvent. Suitable solvents are in principle all solvents which dissolve the monomers used, for example water, alcohols, such as lower alkanols, for example ethanol or methanol, furthermore carboxamides, such as dimethylformamide, dipolar aprotic solvents, such as dimethyl sulfoxide or methyl ethyl ketone, ketones, for example acetone or cyclohexanone, hydrocarbons, for example toluene, ethers, for example THF, dimethoxyethane or dioxane, halogenated hydrocarbons, for example trichloroethane, and also mixtures of suitable solvents, for example mixtures of water and an alcohol, for example a water/ethanol or water/methanol mixture.

A polymer network can, if desired, be reinforced by addition of a crosslinking agent, for example a polyunsaturated comonomer (b). In this case, the term crosslinked polymers is used. The invention, therefore, furthermore relates to a crosslinked polymer comprising the product of the polymerization of a macromer of the formula (I), if desired with at least one vinylic comonomer (a) and with at least one comonomer (b).

Examples of typical comonomers (b) are allyl (meth)acrylate, lower alkylene glycol di(meth)acrylate, poly(lower alkylene) glycol di(meth)acrylate, lower alkylene di(meth)acrylate, divinyl ether, divinyl sulfone, di- and trivinylbenzene, trimethylolpropane tri(meth)acrylate, pentaerythritol tetra(meth)acrylate, bisphenol A di(meth)acrylate, methylenebis(meth)acrylamide, triallyl phthalate and diallyl phthalate.

The amount of comonomer (b) used is expressed in a proportion by weight based on the total polymer and is in the range from 20 to 0.05%, in particular in the range from 10 to 0.1%, preferably in the range from 2 to 0.1%.

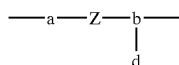
3. Material "C"

Material "C" polymers are formed by polymerizing polymerizable macromers which contain free hydroxyl groups. Macromers which are built up, for example, from an amino-alkylated polysiloxane which is derivatized with at least one polyol component containing an unsaturated polymerizable side chain are disclosed. Polymers can be prepared on the one hand from the macromers according to the invention by homopolymerization. The macromers mentioned furthermore can be mixed and polymerized with one or more hydrophilic and/or hydrophobic comonomers. A special property of the macromers according to the invention is that they function as the element which controls microphase separation between selected hydrophilic and hydrophobic components in a crosslinked end product. The hydrophilic/hydrophobic microphase separation is in the region of less than 300 nm. The macromers are preferably crosslinked at the phase boundaries between, for example, an acrylate comonomer on the one hand and an unsaturated polymerizable side chain of polyols bonded to polysiloxane on the other hand, by covalent bonds and additionally by reversible physical interactions, for example hydrogen bridges. These are formed, for example, by numerous amide or urethane groups. The continuous siloxane phase which exists in the phase composite has the effect of producing a surprisingly high permeability to oxygen.

US 6,951,894 B1

29

The present embodiment of the invention relates to a macromer comprising at least one segment of the formula (I):



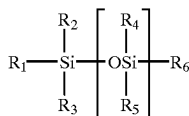
in which

- (a) is a polysiloxane segment,
- (b) is a polyol segment which contains at least 4 C atoms, Z is a segment (c) or a group X_1 ,
- (c) is defined as $X_2\text{---R---}X_2$, wherein R is a bivalent radical of an organic compound having up to 20 C atoms and each X_2 independently of the other is a bivalent radical which contains at least one carbonyl group, X_1 is defined as X_2 , and
- (d) is a radical of the formula (II):



in which

- P_1 is a group which can be polymerized by free radicals; Y and X_3 independently of one another are a bivalent radical which contains at least one carbonyl group; k is 0 or 1; and
 - L is a bond or a divalent radical having up to 20 C atoms of an organic compound.
- A polysiloxane segment (a) is derived from a compound of the formula (III):



in which

- n is an integer from 5 to 500;
 - 99.8–25% of the radicals R_1 , R_2 , R_3 , R_4 , R_5 and R_6 independently of one another are alkyl and 0.2–75% of the radicals R_1 , R_2 , R_3 , R_4 , R_5 and R_6 independently of one another are partly fluorinated alkyl, aminoalkyl, alkenyl, aryl, cyanoalkyl, $\text{alk---NH---alk---NH}$, or $\text{alk---(OCH}_2\text{)}_m\text{---(OCH}_2\text{)}_p\text{---OR}_7$,
 - R_7 is hydrogen or lower alkyl, alk is alkylene, and m and p independently of one another are an integer from 0 to 10, one molecule containing at least one primary amino or hydroxyl group.
- The alkylenoxy groups $\text{---(OCH}_2\text{CH}_2\text{)}_m$ and $\text{---(OCH}_2\text{)}_p$ in the siloxane of the formula (III) are either distributed randomly in a ligand $\text{alk---(OCH}_2\text{CH}_2\text{)}_m\text{---(OCH}_2\text{)}_p\text{---OR}_7$ or are distributed as blocks in a chain. A polysiloxane segment (a) is linked a total of 1–50 times, preferably 2–30 times, and in particular 4–10 times, via a group Z with a segment (b) or another segment (a), Z in an a-Z-a sequence always being a segment (c). The linkage site in a segment (a) with a group Z is an amino or hydroxyl group reduced by one hydrogen.

In a preferred embodiment, a polysiloxane segment is derived from a compound of the formula (III) in which the radicals R_1 , R_2 , R_3 , R_4 , R_5 and R_6 are a total of 1–50 times, more preferably 2–30 times, and in particular 4–10 times,

30

independently either terminally or pendently aminoalkyl or hydroxyalkyl, the other variables being as defined above.

- In a preferred embodiment, a polysiloxane segment is derived from a compound of the formula (III) in which 95–29% of the radicals R_1 , R_2 , R_3 , R_4 , R_5 and R_6 independently of one another are alkyl and 5–71% of the radicals R_1 , R_2 , R_3 , R_4 , R_5 and R_6 independently of one another are partly fluorinated alkyl, aminoalkyl, alkenyl, aryl, cyanoalkyl, $\text{alk---NH---alk---NH}_2$ or $\text{alk---(OCH}_2\text{CH}_2\text{)}_m\text{---(OCH}_2\text{)}_p\text{---OR}_7$, and in which the variables are as defined above.

In a preferred meaning, n is an integer from 5 to 400, more preferably 10 to 250 and particularly preferably 12 to 125.

- In a preferred meaning, the two terminal radicals R_1 and R_6 are aminoalkyl or hydroxyalkyl, the other variables being as defined above. P In another preferred meaning, the radicals R_4 and R_5 are 1–50 times, more preferably 2–30 times and in particular 4–10 times pendently aminoalkyl or hydroxyalkyl and the other variables are as defined above.

- In another preferred meaning, the radicals R_1 , R_2 , R_3 , R_4 , R_5 and R_6 are a total of 1–50 times, more preferably 2–30 times and in particular 4–10 times, independently both terminally and pendently aminoalkyl or hydroxyalkyl and the other variables are as defined above.

If Z is X_1 , X_1 is a bivalent group which contains at least one carbonyl group. A carbonyl group mentioned is flanked in any manner, if appropriate, by ---O--- , ---CONH--- , ---NHCO--- or ---NH--- .

- Examples of bivalent groups Z are typically carbonyls, esters, amides, urethanes, ureas or carbonates.

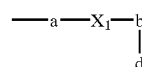
X_1 is preferably an ester, amide, urethane or urea group, in particular an ester or amide group.

- X_2 is defined in the same way as X_1 and is preferably an ester, amide, urethane, carbonate or urea group, more preferably an ester, amide, urethane or urea group and in particular an amide, urethane or urea group.

- If Z in formula (I) is X_1 , a polyol segment b is preferably understood as meaning a polyol derived from a carbohydrate, carbohydrate monolactone or carbohydrate dilactone. A carbohydrate is understood as meaning a mono-, di-, tri-, tetra-, oligo- or polysaccharide. A carbohydrate lactone is understood as meaning the lactone of an aldonic or uronic acid. An aldonic or uronic acid is, for example, a carboxylic acid formed by oxidation of a mono-, di-, tri-, tetra-, oligo- or polysaccharide. Examples of aldonic acid lactones are gluconolactone, galactonolactone, lactobionolactone or maltoheptaonolactone; examples of uronic acid lactones are glucuronic acid lactone, mannuronic acid lactone or iduronic acid lactone. An example of a carbohydrate dilactone is D-glucaro-1,4:6,3-dilactone.

A carbohydrate lactone reacts, for example, with a primary amino group or a hydroxyl group of segment (a) to form a covalent amide or ester bond of the type X_1 . Such linkages are the constituent of a further preferred embodiment of macromers according to the invention. Such macromers have an alternating distribution of segments of type (a) and (b) which are interrupted by X_1 .

- This embodiment of the invention preferably relates to a macromer of the formula (IV):



(IV)

in which the variables are as defined above.

US 6,951,894 B1

31

An embodiment of the invention furthermore preferably relates to a macromer according to formula (V):



in which

the polysiloxane segment (a) contains q pendent ligands x is 0, 1 or 2,

q has an average numerical value of 1–20, preferably 1–10, and in particular 1–5, and

the segments (b) in a macromer according to the formula (V) are linked in total (per molecule) with up to 20, preferably with up to 15, and in particular with up to 6 polymerizable segments (d).

An embodiment of the invention furthermore preferably relates to a macromer according to formula (VI):



in which

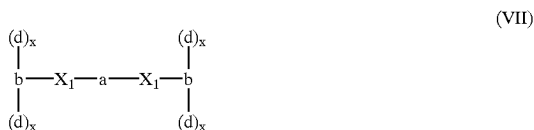
a linear sequence is present,

x is 0, 1 or 2,

q has an average numerical value of 1–20, preferably 1–10, and in particular 1–5, and

the segments (b) in a macromer according to the formula (VI) are linked in total (per molecule) with up to 20, preferably with up to 15, and in particular with up to 6 polymerizable segments (d).

An embodiment of the invention furthermore very preferably relates to a macromer according to formula (VII):



in which x is 0, 1 or 2, and

the average number of segments (d) per molecule of the formula (VII) is preferably in the range from 2 to 5, and very preferably is in the range from 3 to 4.

A polyol segment (b) is derived from a polyol which carries no lactone group if the group Z is a segment (c). Examples of such polyols are a 1,2-polyol, for example the reduced monosaccharides, for example mannitol, glucitol, sorbitol or iditol, a 1,3-polyol, for example polyvinyl alcohol (PVA), which is derived from partly or completely hydrolysed polyvinyl acetate, and furthermore amino-terminal PVA telomers, aminopolyols, aminocyclodextrins, aminomono-, -di-, -tri-, -oligo- or -polysaccharides or cyclodextrin derivatives, for example hydroxypropylcyclodextrin. An abovementioned carbohydrate dilactone can be reacted, for example, with preferably 2 equivalents of an amino-terminal PVA telomer to give a polyol macromer which carries, in the central part, the carbohydrate compound derived from the dilactone. Such polyols of this composition are likewise understood to be a suitable polyol.

As illustrated in formula (I), a segment (b) carries at least one vinylic polymerizable segment (d), a linkage of a segment (d) via the bivalent radical X₃ thereof to an amino or hydroxyl group, of a segment (b), reduced by a hydrogen atom being intended.

32

A vinylic polymerizable segment (d) is incorporated either terminally or pendently preferably 1–20 times, more preferably 2–15 times, and in particular 2–6 times, per macromer molecule according to the invention.

A vinylic polymerizable segment (d) is incorporated terminally and also pendently as desired (as a terminal/pendent mixture) preferably 1–20 times, more preferably 2–15 times and in particular 2–6 times, per macromer molecule according to the invention.

A group P₁ which can be polymerized by free radicals is, for example, alkenyl, alkenylaryl or alkenylarylenealkyl having up to 20 C atoms. Examples of alkenyl are vinyl, allyl, 1-propen-2-yl, 1-buten-2- or -3- or -4-yl, 2-buten-3-yl and the isomers of pentenyl, hexenyl, octenyl, decenyl or undecenyl. Examples of alkenylaryl are vinylphenyl, vinyl-naphthyl or allylphenyl. An example of alkenylarylenealkyl is vinylbenzyl.

P₁ is preferably alkenyl or alkenylaryl having up to 12 C atoms, more preferably alkenyl having up to 8 C atoms and in particular alkenyl having up to 4 C atoms.

L is preferably alkylene, arylene, a saturated bivalent cycloaliphatic group having 6 to 20 carbon atoms, arylenealkylene, alkylenearylene, alkylenearylenealkylene or arylenealkylenearylene. In a preferred meaning, L furthermore is preferably a bond.

In a preferred meaning, L is a divalent radical having up to 12 C atoms, and more preferably a divalent radical having up to 8 C atoms. In a preferred meaning, L furthermore is alkylene or arylene having up to 12 C atoms. A very preferred meaning of L is lower alkylene, in particular lower alkylene having up to 4 C atoms.

Y is preferably a carbonyl, ester, amide or urethane group, in particular a carbonyl, ester or amide group, and very preferably a carbonyl group.

In another preferred meaning, Y is absent, i.e., k is 0.

In a preferred meaning, X₃ is a urethane, urea, ester, amide or carbonate group, more preferably a urethane, urea, ester or amide group, and in particular a urethane or urea group. A vinylic polymerizable segment (d) is derived, for example, from acrylic acid, methacrylic acid, methacryloyl chloride, 2-isocyanatoethyl methacrylate (IEM), allyl isocyanate, vinyl isocyanate, the isomeric vinylbenzyl isocyanates or adducts of hydroxyethyl methacrylate (HEMA) and 2,4-tolylene diisocyanate (TDI) or isophorone diisocyanate (IPDI), in particular the 1:1 adduct. The invention furthermore preferably relates to a macromer in which a segment (d) is incorporated either terminally or pendently or as a terminal/pendent mixture 5 times. The invention furthermore preferably relates to a macromer in which a segment (d) is incorporated terminally 5 times.

The diradical R is, for example, alkylene, arylene, alkylenearylene, arylenealkylene or arylenealkylenearylene having up to 20 carbon atoms, a saturated bivalent cycloaliphatic group having 6 to 20 carbon atoms or cycloalkylenealkylenecycloalkylene having 7 to 20 carbon atoms.

In a preferred meaning, R is alkylene, arylene, alkylenearylene, arylenealkylene or arylenealkylenearylene having up to 14 carbon atoms or a saturated bivalent cycloaliphatic group having 6 to 14 carbon atoms.

In a preferred meaning, R is alkylene, arylene, alkylenearylene or arylenealkylene having up to 14 carbon atoms, or a saturated bivalent cycloaliphatic group having 6 to 14 carbon atoms. In a preferred meaning, R is alkylene or arylene having up to 12 carbon atoms, or a saturated bivalent cycloaliphatic group having 6 to 14 carbon atoms.

In a preferred meaning, R is alkylene or arylene having up to 10 carbon atoms, or is a saturated bivalent cycloaliphatic group having 6 to 10 carbon atoms.

US 6,951,894 B1

33

In a very preferred meaning, a segment (c) is derived from a diisocyanate, for example from hexane 1,6-diisocyanate, 2,2,4-trimethylhexane 1,6-diisocyanate, tetramethylene diisocyanate, phenylene 1,4-diisocyanate, toluene 2,4-diisocyanate, toluene 2,6-diisocyanate, m- or p-tetramethylxylene diisocyanate, isophorone diisocyanate or cyclohexane 1,4-diisocyanate.

A preferred embodiment of segment (c) is furthermore derived from a diisocyanate in which the isocyanate groups have different reactivities. The different reactivity is influenced, in particular, by the spatial requirements and/or electron density in the neighbourhood of an isocyanate group.

The average molecular weight of a macromer according to the invention is preferably in the range from about 300 to about 30,000, very preferably in the range from about 500 to about 20,000, more preferably in the range from about 800 to about 12,000, and particularly preferably in the range from about 1000 to about 10,000.

A preferred embodiment of the macromer has a segment sequence of the formula (VIII):



in which

r is an integer from 1 to 10, preferably from 1 to 7, and in particular from 1 to 3;

t is 0 or 1, and preferably 1;

a linear (c-a) chain which may or may not be terminated by a segment (b) is present (t=1); and

the above preferences apply to the total number of segments (d), which are preferably bonded to a segment (b).

A preferred embodiment of the macromer has a segment sequence of formula (IX):



in which

the sequence (c-a)-(Z-b)_t hangs pendently r times on the segment (a) and may or may not be terminated by a segment (b);

r is an integer from 1 to 10, preferably from 1 to 7, and in particular from 1 to 3;

t is 0 or 1, and is preferably 1;

Z is a segment (c) or a group X₁; and

the above preferences apply to the total number of segments (d), which are preferably bonded to a segment (b).

Another preferred embodiment of the macromer has a segment sequence of formula (X):



in which

s is an integer from 1 to 10, preferably from 1 to 7, and in particular from 1 to 3;

B is a segment (a) or (b); and

the above preferences apply to the number of segments (d), which are bonded to a segment (b).

Another preferred embodiment of the macromer has a segment sequence of the formula (XI):



in which

the structures are linear,

s is an integer from 1 to 10, preferably from 1 to 7, and in particular from 1 to 3;

34

B is a segment (a) or (b);

t is 0 or 1, and

the above preferences apply to the number of segments (d), which are bonded to a segment (b).

The ratio of the number of segments (a) and (b) in a macromer according to the Material "C" embodiment of the invention is preferably in a range of (a):(b)=3:4, 2:3, 1:2, 1:1, 1:3 or 1:4. The total sum of segments (a) and (b) or, where appropriate, (a) and (b) and (c) is in a range from 2 to 50, preferably 3 to 30, and in particular in the range from 3 to 12.

Alkyl has up to 20 carbon atoms and can be straight-chain or branched. Suitable examples include dodecyl, octyl, hexyl, pentyl, butyl, propyl, ethyl, methyl, 2-propyl, 2-butyl or 3-pentyl.

Arylene is preferably phenylene or naphthylene, which is unsubstituted or substituted by lower alkyl or lower alkoxy, in particular 1,3-phenylene, 1,4-phenylene or methyl-1,4-phenylene; or 1,5-naphthylene or 1,8-naphthylene.

Aryl is a carbocyclic aromatic radical, which is unsubstituted or substituted by preferably lower alkyl or lower alkoxy. Examples are phenyl, toluyl, xylyl, methoxyphenyl, t-butoxyphenyl, naphthyl or phenanthryl.

A saturated bivalent cycloaliphatic group is preferably cycloalkylene, for example cyclohexylene or cyclohexylene-lower alkylene, for example cyclohexylenemethylene, which is unsubstituted or substituted by one or more lower alkyl groups, for example methyl groups, for example trimethylcyclohexylenemethylene, for example the bivalent isophorone radical. The term "lower" in the context of this invention in connection with radicals and compounds, unless defined otherwise, means, in particular, radicals or compounds having up to 8 carbon atoms, preferably having up to 4 carbon atoms.

Lower alkyl has, in particular, up to 8 carbon atoms, preferably up to 4 carbon atoms, and is, for example, methyl, ethyl, propyl, butyl, tert-butyl, pentyl, hexyl or isohexyl.

Alkylene has up to 12 carbon atoms and can be straight-chain or branched. Suitable examples include decylene, octylene, hexylene, pentylene, butylene, propylene, ethylene, methylene, 2-propylene, 2-butylenes or 3-pentylene.

Lower alkylene is alkylene having up to 8, and particularly preferably having up to 4 carbon atoms. Particularly preferred examples of lower alkyls are propylene, ethylene and methylene.

The arylene unit of alkylenearylene or arylenealkylene is preferably phenylene, which is unsubstituted or substituted by lower alkyl or lower alkoxy, and the alkylene unit of this is preferably lower alkylene, such as methylene or ethylene, in particular methylene. Such radicals are therefore preferably phenylenemethylene or methylenephenylene.

Lower alkoxy has, in particular, up to 8 carbon atoms, preferably up to 4 carbon atoms, and is, for example, methoxy, ethoxy, propoxy, butoxy, tert-butoxy or hexyloxy.

Partly fluorinated alkyl is understood as meaning alkyl in which up to 90%, preferably up to 70%, and in particular up to 50%, of the hydrogens are replaced by fluorine.

Arylenealkylenearylene is preferably phenylene-lower alkylene-phenylene having up to 8, and in particular having up to 4 carbon atoms in the alkylene unit, for example phenylenemethylenephenylene or phenylenemethylenephenylene.

A monosaccharide in the context of the present invention is understood as meaning an aldopentose, aldohexose, aldotetrose, ketopentose or ketohexose.

US 6,951,894 B1

35

Examples of an aldopentose are D-ribose, D-arabinose, D-xylose or D-lyxose; examples of an aldohexose are D-allose, D-altrose, D-glucose, D-mannose, D-gulose, D-idose, D-galactose, D-talose, L-fucose or L-rhamnose; examples of a ketopentose are D-ribulose or D-xylulose; examples of a tetrose are D-erythrose or threose; and examples of a ketohexose are D-psicose, D-fructose, D-sorbose or D-tagatose. Examples of a disaccharide are trehalose, maltose, somaltose, cellobiose, gentiobiose, saccharose, lactose, chitobiose, N,N-diacetylchitobiose, palatinose or sucrose. Raffinose, panose or maltotriose may be mentioned as an example of a trisaccharide. Examples of an oligosaccharide are maltotetraose, maltohexaose, chitoheptaose and furthermore cyclic oligosaccharides, such as cyclodextrins.

Cyclodextrins contain 6 to 8 identical units of α -, β - and γ -cyclodextrin, derivatives of such cyclodextrins, for example hydroxypropylcyclodextrins, and branched cyclodextrins.

The macromers according to this embodiment of invention can be prepared by processes known per se, for example as follows.

In a first step, a polysiloxane containing at least one primary amino- or hydroxyalkyl group is reacted with a carbohydrate lactone, an amide or ester bond being formed and a compound of the formula (XIIa) or (XIIb) being formed:



in which the variables are as defined above and Z is a group XI, after which the compound (XII) is reacted with an unsaturated polymerizable compound of the formula (XII):



in which X_4 is a group which is coreactive with a hydroxyl or amino group of segment (b), an X_3 group of a segment (d) according to formula (II) being formed from such a reaction, where X_4 is preferably $-\text{COOH}$, $-\text{COOR}_{10}$, $-\text{COCl}$ or $-\text{NCO}$, in which R_{10} is alkyl, or is aryl which is unsubstituted or substituted by lower alkyl or lower alkoxy, and the other variables are as defined above, after which a macromer according to the formula (IV) or (V) is formed



in which the segments (d) are incorporated terminally or pendently.

Another process starts from a polysiloxane (a) which contains terminal primary amino- or hydroxyalkyl groups and is reacted with a carbohydrate dilactone to form linear structures of the formula (XIV):



in which the variables are as defined and preferred above, after which a compound of the formula (XIV) is reacted with

36

a compound of the formula (XIII) analogously to the above process to give a macromer of the formula (VI):

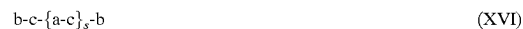


in which the variables are as defined and preferred above.

Another process starts from a polysiloxane (a) which contains terminal primary amino- or hydroxyalkyl groups and is initially reacted with a bifunctional compound of the formula (XV):



in which X_4 is a group which is coreactive with a hydroxyl or amino group of segment (a), an X_2 group of a segment (c) being formed from such a reaction, where X_4 is preferably $-\text{COOH}$, $-\text{COOR}_{10}$, $-\text{COCl}$ or $-\text{NCO}$, in which R_{10} is alkyl, or aryl which is unsubstituted or substituted by lower alkyl or lower alkoxy, and R is as defined above, after which this intermediate is reacted with a polyol which carries no lactone group to give a compound of the formula (XVI):



in which the variables are as defined and preferred above, after which the compound of the formula (XVI) is reacted with a compound of the formula (XIII) to give a macromer of the formula (X):



in which s is an integer from 1 to 10, preferably from 1 to 7, and in particular from 1 to 3; B is a segment (a) or (b); and the above preferences apply to the number of segments (d) which are bonded to a segment (b).

Another process starts from a bifunctional compound of the formula (XV):



in which is reacted with an excess of polysiloxane (a) to give an $-a-(c-a)-$ sequence, in which the above meanings apply, after which, in a second step, the intermediate is reacted with a polyol which carries no lactone to give a compound of the formula (XVII):



after which the compound (XVII) is reacted with the compound (XIII) to give a macromer of the formula (VIII):

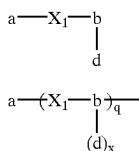


in which r is an integer from 1 to 10, preferably from 1 to 7, and in particular from 1 to 3; t is 0 or 1, and is preferably 1; in which a linear (c-a) chain, which may or may not be terminated by a segment (b), is present (t=1); and the above preferences apply to the total number of segments (d), which are preferably bonded to a segment (b).

Another process starts from a carbohydrate lactone which is reacted in a first step with a compound of the formula (XIII), the lactone function being retained, after which the intermediate is reacted with a polysiloxane containing at least one amino or hydroxyl group to give a compound of the formula (IV) or (V):

US 6,951,894 B1

37



in which q is typically 1 or 2, and in which the above meanings and preferences otherwise apply, and the segments (d) are incorporated terminally or pendently.

The present embodiment of the invention furthermore relates to the intermediates which are novel and which occur during synthesis of the macromers according to the invention.

The invention therefore furthermore relates to a compound of the formula (XIIa):



in which q is greater than 1,

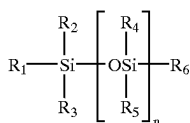
(a) is derived from a polysiloxane as defined by formula (I) above and

(b) is derived from a carbohydrate dilactone.

An embodiment of the invention furthermore relates to a compound of the formula (XIIb):



in which Z, (b) and q are as defined and preferred above, but with the proviso that a segment (a) is derived from a compound of the formula (III):



in which n is an integer from 5 to 500;

99.8–25% of the radicals R_1 , R_2 , R_3 , R_4 , R_5 and R_6 independently of one another are alkyl and

0.2–75% of the radicals R_1 , R_2 , R_3 , R_4 , R_5 and R_6 independently of one another are partly fluorinated alkyl, aminoalkyl, alkenyl, aryl, cyanoalkyl, alk-NH-Alk-NH₂ or alk-(OCH₂CH₂)_m-(OCH₂)_p-OR₇ in which R_7 is hydrogen or lower alkyl, alk is alkylene and

m and p independently of one another are an integer from 0 to 10, one molecule containing at least one primary amino or hydroxyl group and at least one partly fluorinated alkyl group.

The invention furthermore relates to a compound of the formula (XVI):



in which a segment (b) is derived from a polyol which carries no lactone and the other variables are as defined and preferred above.

An embodiment of the invention furthermore relates to a compound of the formula (XVII):



in which a segment (b) is derived from a polyol which carries no lactone and the other variables are as defined and preferred above.

38

(IV) A siloxane (a) containing at least one primary amino or hydroxyl group is, for example, commercially obtainable. Examples are KF-6002, KF-8003, X-22-161C (Shin Etsu) or GP4 (Genesee). Other siloxanes can be synthesized with the aid of published processes.

(V) 5 A polyol (b) required for the synthesis is as a rule commercially obtainable. Examples are gluconolactone or lactobionolactone. Otherwise, they can be synthesized with the aid of a published process.

10 The compounds according to the invention can be prepared in the presence or absence of a solvent. A solvent which is largely inert, i.e., does not participate in the reaction, is advantageously used. Suitable examples of these are ethers, such as tetrahydrofuran (THF), 1,2-dimethoxyethane, diethylene glycol dimethyl ether or dioxane, halogenated hydrocarbons, such as chloroform or methylene chloride, bipolar aprotic solvents, such as acetonitrile, acetone, dimethylformamide (DMF) or dimethyl sulfoxide (DMSO), hydrocarbons, such as toluene or xylene, and furthermore pyridine or N-methylmorpholine.

20 The reactants are advantageously employed in stoichiometric amounts for the preparation of the compounds according to the invention. The reaction temperature can be, for example, from -30° C. to 50° C. The range from 0° C. to 40° C. is a preferred temperature range. The reaction times here are in the range from about 15 minutes to 7 days, preferably in the region of about 12 hours. If necessary, the reaction is carried out under argon or nitrogen as an inert gas. A suitable catalyst is advantageously added for urethane-forming reactions, for example dibutyltin dilaurate (DBTDL).

The present invention furthermore relates to a polymer comprising a polymerization product of at least one macromer according to the invention as defined above and, if appropriate, at least one vinylic comonomer (a).

35 The preferred composition of a polymer according to the invention comprises a weight content, with respect to the total polymer, of a macromer according to the invention in the range from 100 to 0.5%, in particular in the range from 80 to 10%, and preferably in the range from 70 to 30%.

40 In a preferred polymer comprising a polymerization product of at least one macromer according to the invention, comonomer (a) is absent and the polymer is preferably a homopolymer.

45 A comonomer (a) which is contained in a polymer according to the invention can be hydrophilic or hydrophobic or a mixture of both. Suitable comonomers include, in particular, those which are usually used for the preparation of contact lenses and biomedical materials. A hydrophobic comonomer (a) is understood as meaning monomers which typically give, as a homopolymer, polymers which are water-insoluble and can absorb less than 10% by weight of water.

Analogously, a hydrophilic comonomer (a) is understood as meaning a monomer which typically gives, as a homopolymer, a polymer which is water-soluble or can absorb at least 10% by weight of water.

55 Suitable hydrophobic comonomers (a) include, without this list being exhaustive, C₁-C₁₈alkyl and C₃-C₁₈cycloalkyl acrylates and methacrylates, C₃-C₁₈alkylacrylamides and -methacrylamides, acrylonitrile, methacrylonitrile, vinyl C₁-C₁₈alkanoates, C₂-C₁₈alkenes, C₂-C₁₈haloalkenes, styrene, lower alkyl styrene, lower alkyl vinyl ethers, C₂-C₁₀perfluoroalkyl acrylates and methacrylates or correspondingly partly fluorinated acrylates and methacrylates, C₃-C₁₂perfluoroalkylethyl-thiocarbonylaminoethyl acrylates and methacrylates, acryloxy- and methacryloxy-alkylsiloxanes,

US 6,951,894 B1

39

N-vinylcarbazole and C₁-C₁₂alkyl esters of maleic acid, fumaric acid, itaconic acid, mesaconic acid and the like. Preferred comonomers are, for example, acrylonitrile, C₁-C₄alkyl esters of vinylically unsaturated carboxylic acids having 3 to 5 carbon atoms, or vinyl esters of carboxylic acids having up to 5 carbon atoms.

Examples of suitable hydrophobic comonomers (a) include methyl acrylate, ethyl acrylate, propyl acrylate, isopropyl acrylate, isobutyl acrylate (IBA), isooctyl acrylate (OA), isodecyl acrylate (DA), cyclohexyl acrylate, 2-ethylhexyl acrylate (EHA), methyl methacrylate, ethyl methacrylate, propyl methacrylate, butyl acrylate, vinyl acetate, vinyl propionate, vinyl butyrate, vinyl valerate, styrene, chloroprene, vinyl chloride, vinylidene chloride, acrylonitrile, 1-butene, butadiene, methacrylonitrile, vinyl toluene, vinyl ethyl ether, perfluorohexylethylthiocarbonylaminoethyl methacrylate, isobornyl methacrylate, trifluoroethyl methacrylate, hexafluoroisopropyl methacrylate, hexafluorobutyl (meth)acrylate (HFBMA and HFBA), tris(trimethylsilyloxy-silyl-propyl methacrylate (TRIS), 3-methacryloxypropylpentamethyldisiloxane and bis(methacryloxypropyl) tetramethyldisiloxane. Preferred examples of hydrophobic comonomers (a) are methyl methacrylate, IBA, HFBA, HFBMA, OA, EHA, DA, TRIS and acrylonitrile.

Suitable hydrophilic comonomers (a) include, without this list being conclusive, hydroxyl-substituted lower alkyl acrylates and methacrylates, acrylamide, methacrylamide, lower alkylacrylamides and -methacrylamides, ethoxylated acrylates and methacrylates, hydroxyl-substituted lower alkylacrylamides and -methacrylamides, hydroxyl-substituted lower alkyl vinyl ethers, sodium vinylsulfonate, sodium styrenesulfonate, 2-acrylamido-2-methylpropanesulfonic acid, N-vinylpyrrole, N-vinyl-2-pyrrolidone, 2-vinylloxazoline, 2-vinyl-4,4'-dialkylloxazolin-5-one, 2- and 4-vinylpyridine, vinylically unsaturated carboxylic acids having a total of 3 to 5 carbon atoms, amino-lower alkyl (where the term "amino" also includes quaternary ammonium), mono-lower alkylamino-lower alkyl and di-lower alkylamino-lower alkyl acrylates and methacrylates, allyl alcohol and the like. Preferred comonomers are, for example, N-vinyl-2-pyrrolidone, acrylamide, methacrylamide, hydroxyl-substituted lower alkyl acrylates and methacrylates, hydroxyl-substituted lower alkylacrylamides and -methacrylamides and vinylically unsaturated carboxylic acids having a total of 3 to 5 carbon atoms.

Examples of suitable hydrophilic comonomers (a) include hydroxyethyl methacrylate (HEMA), hydroxyethyl acrylate, hydroxypropyl acrylate, trimethylammonium 2-hydroxypropyl methacrylate hydrochloride (Blemer®QA, for example from Nippon Oil), dimethylaminoethyl methacrylate (DMAEMA), dimethylaminoethyl methacrylamide, acrylamide, methacrylamide, N,N-dimethylacrylamide (DMA), allyl alcohol, vinylpyridine, glycerol methacrylate, N-(1,1-dimethyl-3-oxobutyl)acrylamide, N-vinyl-2-pyrrolidone (NVP), acrylic acid, methacrylic acid and the like.

Preferred hydrophilic comonomers (a) are 2-hydroxyethyl methacrylate, dimethylaminoethyl methacrylate, trimethylammonium-2-hydroxypropyl methacrylate hydrochloride, N,N-dimethylacrylamide and N-vinyl-2-pyrrolidone.

The polymers according to the invention are built up in a manner known per se from the corresponding monomers (the term monomers here also including a macromer according to the invention) by a polymerization reaction with

40

which the expert is familiar. Usually, a mixture of the abovementioned monomers is heated, with the addition of an agent which forms free radicals. Such an agent which forms free radicals is, for example, azoisobutyronitrile (AIBN), potassium peroxodisulfate, dibenzoyl peroxide, hydrogen peroxide or sodium percarbonate. If the compounds mentioned are heated, for example, free radicals are then formed, by homolysis, and can then, for example, initiate a polymerization.

A polymerization reaction can particularly preferably be carried out using a photoinitiator. Photopolymerization is the term used in this case. For photopolymerization, a photoinitiator which can initiate free radical polymerization and/or crosslinking by the use of light is suitably added. Examples of this are familiar to the expert, and specifically, suitable photoinitiators are benzoin methyl ether, 1-hydroxycyclohexyl phenyl ketone and Darocur and Irgacur types, preferably Darocur 1173® and Darocur 2959®. Reactive photoinitiators which can be incorporated, for example, into a macromer or can be used as a special comonomer (a) are also suitable. Examples of these are to be found in EP 632 329. The photopolymerization can then be triggered off by actinic radiation, for example light, in particular UV light of a suitable wavelength. The spectral requirements can be controlled accordingly, if appropriate, by addition of suitable photosensitizers.

Polymerization can be carried out in the presence or absence of a solvent. Suitable solvents are in principle all solvents which dissolve the monomers used, for example water, alcohols, such as lower alkanols, for example ethanol or methanol, and furthermore carboxylic acid amides, such as dimethylformamide, dipolar aprotic solvents, such as dimethyl sulfoxide or methyl ethyl ketone, ketones, for example acetone or cyclohexanone, hydrocarbons, for example toluene, ethers, for example THF, dimethoxyethane or dioxane, and halogenated hydrocarbons, for example trichloroethane, and also mixtures of suitable solvents, for example mixtures of water with an alcohol, for example a water/ethanol or a water/methanol mixture.

If appropriate, a polymer network can be intensified by addition of a so-called crosslinking agent, for example a polyunsaturated comonomer (b). The invention furthermore relates to a polymer comprising the polymerization product of a macromer according to the invention with, if appropriate, at least one vinylic comonomer (a) and with at least one comonomer (b).

Examples of typical comonomers (b) are, for example, allyl(meth)acrylate, lower alkylene glycol di(meth)acrylate, poly lower alkylene glycol di(meth)acrylate, lower alkylene di(meth)acrylate, divinyl ether, divinyl sulfone, di- or trivinylbenzene, trimethylolpropane tri(meth)acrylate, pentaerythritol tetra(meth)acrylate, bisphenol A di(meth)acrylate, methylenebis(meth)acrylamide, triallyl phthalate or diallyl phthalate.

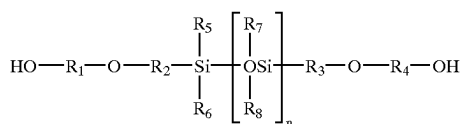
The amount of comonomer (b) used is expressed in the weight content with respect to the total polymer and is in the range from 20 to 0.05%, in particular in the range from 10 to 0.1%, and preferably in the range from 2 to 0.1%.

4. "Material D"

Another advantageous embodiment of the present invention relates to the use of a siloxane-containing macromer which is formed from a poly(dialkylsiloxane) dialkoxyalkanol having the following structure:

US 6,951,894 B1

41



where n is an integer from about 5 to about 500, preferably about 20 to 200, more preferably about 20 to 100;

the radicals R₁, R₂, R₃, and R₄, independently of one another, are lower alkylene, preferably C₁-C₆ alkylene, more preferably C₁-C₃ alkylene, wherein in a preferred embodiment, the total number of carbon atoms in R₁ and R₂ or in R₃ and R₄ is greater than 4; and

R₅, R₆, R₇, and R₈ are, independently of one another, are lower alkyl, preferably C₁-C₆ alkyl, more preferably C₁-C₃ alkyl.

The general structure of the Material D macromer follows:

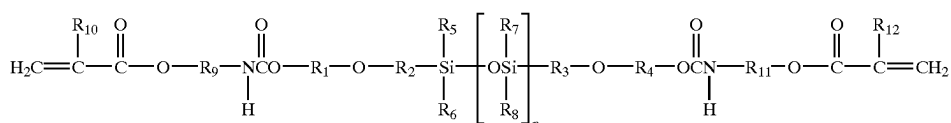


where the ACRYLATE is selected from acrylates and methacrylates; LINK is selected from urethanes and dirurethane linkages, ALK-O-ALK is as defined above (R₁-O-R₂ or R₃-O-R₄), and PDAS is a poly(dialkylsiloxane).

For example, a Material D macromer may be prepared by reacting isophorone diisocyanate, 2-hydroxyethyl (meth)acrylate and a poly(dialkylsiloxane) dialkoxyalkanol in the presence of a catalyst.

A preferred Material D macromer may be prepared by reacting a slight excess of isocyanatoalkyl methacrylate, especially isocyanatoethyl methacrylate (IEM), with a poly(dialkylsiloxane) dialkoxyalkanol, preferably poly(dimethylsiloxane) dipropoxyethanol, in the presence of a catalyst, especially an organotin catalyst such as dibutyltin dilaurate (DBTL).

The primary resulting structure is as follows:



where R₉ and R₁₁ are alkylene; preferably C₁₋₆ alkylene, more preferably ethylene; R₁₀ and R₁₂ are methyl or hydrogen.

The "Material D" prepolymer mixture may be formed by mixing the aforementioned siloxane-containing macromer with one or more hydrophilic monomers and a thermoinitiator or a photoinitiator such as Darocur®1173. A solvent, such as hexanol, is preferably added to homogenize the mixture. Preferably, an appropriate amount of TRIS is added to lower the modulus of elasticity to a desired level. The ionperm monomer or monomers may be selected from any of the aforementioned ionperm or hydrophilic monomers. Preferably, the ionperm monomer is selected from the group consisting of acrylates, methacrylates, acrylamides, methacrylamides and mixtures thereof. More preferably, the ionperm monomers are selected from dimethylacrylamide (DMA) and methacrylic acid (MAA).

A preferred "Material D" prepolymer mixture, in weight percentages based on total mixture weight, includes about 35 to 60% Material D macromer; about 6 to 25% TRIS; about

42

15 to 35% ionperm monomer; about 0.1 to 1% photoinitiator; and about 10 to 20% solvent. A more preferred "Material D" prepolymer mixture, in weight percentages based on total mixture weight, includes the following: about 40 to 55% Material D macromer; about 8 to 16% TRIS; about 20 to 30% dimethylacrylamide; about 0.2 to 2% methacrylic acid; about 0.1 to 1% photoinitiator; and about 10 to 20% solvent. A particularly preferred "Material D" prepolymer mixture, in weight percentages based on total mixture weight, includes the following: about 44 to 50% Material D macromer; about 10 to 12% TRIS; about 22 to 26% dimethylacrylamide; about 0 to 1% methacrylic acid; about 0.2 to 0.6% photoinitiator; and about 10 to 20% solvent.

The prepolymer mixture may be formed into lenses and other ophthalmic devices by any of a number of techniques known in the art and disclosed herein. Preferably, the prepolymer mixture is conveyed into a concave half of a lens mold, the convex mold half is mated with the concave mold half, and an appropriate amount of radiation is applied to initiate polymerization. While ultraviolet (UV) radiation is preferred, a number of other energy sources known in the art and disclosed herein may also be used.

The Material D ophthalmic lens is preferably a polymerization product of the following macromeric and monomeric components, based on total weight of polymerizable material:

- (a) about 45 to about 65 percent Material D macromer;
- (b) about 5 to about 25 percent TRIS; and
- (c) about 20 to about 40 percent ionperm monomer.

The Material D ophthalmic lens is more preferably a polymerization product of the following macromeric and monomeric components, based on total weight of polymerizable material:

- (a) about 50 to about 60 percent Material D macromer;
- (b) about 10 to about 20 percent TRIS; and
- (c) about 25 to about 35 percent ionperm monomer.

In a preferred embodiment, the Material D ophthalmic lens is a polymerization product of the following macro-

meric and monomeric components, based on total weight of polymerizable material:

- (a) about 50 to about 60 percent Material D macromer;
- (b) about 10 to about 20 percent TRIS;
- (c) about 25 to about 35 percent DMA; and
- (d) up to about 2 percent MAA.

In another preferred embodiment, about 0.2 to 1.0 weight percent MAA is used, together with the components (a), (b), and (c) in the above-cited amounts.

III. OPHTHALMICALLY COMPATIBLE SURFACES

The ophthalmic lenses of the present invention have a surface which is biocompatible with ocular tissue and ocular fluids during the desired extended period of contact. In one preferred embodiment, the ophthalmic lenses of the present invention include a core material, as defined above, surrounded, at least in part, by a surface which is more hydrophilic and lipophobic than the core material. A hydrophilic surface is desirable in order to enhance the compatibility of the lens with the ocular tissues and tear fluids. As

US 6,951,894 B1

43

surface hydrophilicity increases, undesirable attraction and adherence of lipids and proteinaceous matter typically decreases. There are factors other than surface hydrophilicity, such as immunological response which may contribute to deposit accumulation on the lens. Deposition of lipids and proteinaceous matter causes haze on the lens, thereby reducing visual clarity. Proteinaceous deposits may also cause other problems, such as irritation to the eye. After extended periods of continuous or intermittent wear, the lens must be removed from the eye for cleaning, i.e., deposit removal. Therefore, increased surface hydrophilicity, and concomitant reductions in deposits of biological matter, allows increased wear time.

"Surface treatment processes" as used herein, refers to processes to render a surface more ophthalmically compatible, in which, by means of contact with a vapor or liquid, and/or by means of application of an energy source (1) a coating is applied to the surface of an article, (2) chemical species are adsorbed onto the surface of an article, (3) the chemical nature (e.g., electrostatic charge) of chemical groups on the surface of an article are altered, or (4) the surface properties of an article are otherwise modified.

There are a variety of methods disclosed in the art for rendering a surface of a material hydrophilic. For example, the lens may be coated with a layer of a hydrophilic polymeric material. Alternatively, hydrophilic groups may be grafted onto the surface of the lens, thereby producing a monolayer of hydrophilic material. These coating or grafting processes may be effected by a number of processes, including without limitation thereto, exposing the lens to plasma gas or immersing the lens in a monomeric solution under appropriate conditions.

Another set of methods of altering the surface properties of a lens involves treatment prior to polymerization to form the lens. For example, the mold may be treated with a plasma (i.e., an ionized gas), a static electrical charge, irradiation, or other energy source, thereby causing the prepolymerization mixture immediately adjacent the mold surface to differ in composition from the core of the prepolymerization mixture.

A preferred class of surface treatment processes are plasma processes, in which an ionized gas is applied to the surface of an article. Plasma gases and processing conditions are described more fully in U.S. Pat. Nos. 4,312,575 and 4,632,844, which are incorporated herein by reference. The plasma gas is preferably a mixture of lower alkanes and nitrogen, oxygen or an inert gas.

In a preferred embodiment, the lens is plasma treated in the presence of a mixture of (a) a C_{1-6} alkane and (b) a gas selected from the group consisting of nitrogen, argon, oxygen, and mixtures thereof. In a more preferred embodiment, the lens is plasma treated in the presence of a mixture of methane and air.

IV. UTILITY

A. Ophthalmic Lenses

The novel polymers or crosslinked polymers can be converted into ophthalmic moldings in a manner known in the art, in particular into contact lenses, for example by carrying out the photopolymerization or photocrosslinking of the novel polymers in a suitable contact lens mold. Examples of novel ophthalmic moldings, in addition to contact lenses, include without limitation thereto, contact lenses for vision correction, contact lenses for eye color modification, ophthalmic drug delivery devices, ophthalmic wound healing devices, and the like.

B. Contact Lenses

A specific embodiment of the invention is directed to contact lenses which comprise essentially a novel polymer

44

or polymeric network. Such contact lenses have a range of unusual and extremely advantageous properties. Amongst these properties are, for example, their excellent compatibility with the human cornea (if necessary after suitable surface treatment (coating)) and with tear fluid, which is based on a balanced ratio between water content and water permeability, oxygen permeability and mechanical and adsorptive properties. This balance of desirable properties results in high comfort and the absence of irritation and allergenic effects. Owing to their favorable permeability properties with respect to various salts, nutrients, water and diverse other components of tear fluid and gases (CO_2 and O_2), the novel contact lenses have no effect, or virtually no effect, on the natural metabolic processes in the cornea. In contrast to many other siloxane-containing contact lenses, the present innovative extended-wear lenses have chemical and mechanical properties and ion permeability sufficient to avoid the undesired binding effect. Furthermore, the novel contact lenses have high dimensional stability and shelf life.

It must be emphasized that this balance of properties, especially the high ion permeability in combination with the high oxygen permeability, is key to producing a true extended-wear contact lens. The high oxygen permeability is required to prevent corneal swelling, thereby reducing the likelihood of ocular damage and wearer discomfort during periods of extended wear. The high ion permeability enables the lens to move on the eye such that corneal health is not substantially altered and wearer comfort is acceptable during a period of extended, continuous contact with ocular tissue and ocular fluids.

The preferred extended-wear contact lenses of the present invention are those which are comfortable over the period of extended wear. If the lens diameter is too small, the eyelids will not cover any portion of the lens when the eye is open. Thus, the eyelids will contact the edge of the lens each time the eyelid is closed. This repeated eyelid-lens interaction typically causes irritation, wearer discomfort, and lens dislodgement. Accordingly, the preferred contact lens diameters are those which are sufficiently large to minimize eyelid-lens interaction and the associated irritation. Preferably, the contact lens has a diameter of about 12 to about 16 millimeters, more preferably about 13 to 15 mm, and most preferably about 13.5 to 14.8 mm.

V. METHODS OF USE AS EXTENDED-WEAR LENSES

The above-described ophthalmic lenses have special utility as extended-wear contact lenses. Contact lenses having sufficient oxygen and water transmission rates from inner (base curve) to outer (front curve) surface may be continuously worn for long periods of time without substantial corneal swelling or wearer discomfort. The method of wear includes (a) applying the lens to the eye and (b) allowing the lens to remain in intimate contact with the eye and tear fluids for a period of at least 24 hours without substantial adverse impact on corneal health or wearer comfort.

A preferred method includes additional steps of (c) removing the lens from the ocular environment; (d) treating the lens (i.e., disinfecting or cleaning the lens); (e) re-applying the lens to the eye; and (f) allowing the lens to remain in intimate contact with the eye and tear fluids for a period of at least an additional 24 hours without substantial adverse impact on corneal health or wearer comfort.

In a preferred embodiment, the lens is worn for a continuous period of at least four (4) days without substantial corneal swelling or wearer discomfort. In another preferred embodiment, the lens is worn for a continuous period of at least seven (7) days without substantial corneal swelling or wearer discomfort. In another preferred embodiment, the

US 6,951,894 B1

45

lens is worn for a continuous period of at least 14 days without substantial corneal swelling or wearer discomfort. In yet another preferred embodiment, the lens is worn for a continuous period of at least 30 days without substantial corneal swelling or wearer discomfort

VI. METHODS OF MANUFACTURE

The ophthalmic lens may be manufactured, generally, by thoroughly mixing the oxyperm and ionoperm polymerizable materials applying an appropriate amount of the mixture to a lens mold cavity, and initiating polymerization. Photoinitiators, such as those commercially available photoinitiators disclosed above, may be added to the prepolymerization mixture to aid in initiating polymerization. Polymerization may be initiated by a number of well known techniques, which, depending on the polymerizable material, may include application of radiation such as microwave, thermal, e-beam and ultraviolet. A preferred method of initiating polymerization is by application of ultraviolet radiation.

It has been discovered that the ion and/or water permeability of some of the aforementioned core materials may be increased by initiating and completing polymerization in an atmosphere which is substantially free of oxygen. Suitable gases which are readily commercially available include, without limitation thereto, nitrogen and carbon dioxide. Thus, in a preferred embodiment, the oxyperm and ionoperm polymerizable materials are polymerized in an atmosphere having less than about 10000 ppm oxygen. More preferably, the atmosphere surrounding the polymerizable material contains less than about 1000 ppm oxygen. Even more preferably, the surrounding atmosphere contains less than about 100 ppm oxygen, while the most preferred oxygen content is less than about 20 ppm.

In the aforementioned embodiment, the prepolymer mixture must be degassed prior to polymerization. The degassing may be accomplished by a number of techniques known in the art. One technique for degassing the prepolymer mixture involves the use of a series of freezing and thawing steps which are repeated until the appropriate gas concentration level is achieved in the prepolymer mixture. This freeze/thaw method involves cooling the prepolymer mixture until the mixture solidifies, applying a vacuum to the solidified prepolymer mixture, discontinuing the vacuum, and thawing the prepolymer mixture until the mixture is again in liquid form. While this degassing technique is advantageous in a laboratory setting, other degassing techniques known in the art may be more advantageous for commercial lens manufacturing processes.

Alternatively, the atmosphere surrounding the lens mold may be include oxygen, under certain conditions. For example, if the lens mold halves seal adequately to one another and the lens mold material has a low rate of oxygen permeability (e.g., polypropylene), it is possible to polymerize a degassed prepolymer mixture in a mold surrounded by ambient air without reaching prepolymer oxygen concentrations sufficiently high to substantially reduce ion or water permeability of the final lens. Thus, in another preferred embodiment of double-sided molding, the lens is formed by the following steps: (1) the prepolymer mixture is degassed, (2) a lens mold half is filled with the prepolymer mixture, (3) the mold halves are sealed to one another, and (4) the polymerization is initiated to form the lens, where the lens mold halves are formed from a material having a low oxygen permeability and steps (2)–(4) may occur in the presence or absence of oxygen. In this embodiment, it is preferred that the lens molds are stored in an inert substantially oxygen-free atmosphere, e.g., nitrogen or carbon dioxide, prior to use.

46

An essential feature of the manufacturing methods of the present innovative lenses is that a balance of high oxygen permeability and high ion permeability is achieved. Manufacturing techniques and conditions which result in lowering either the oxygen permeability or the ion permeability below levels sufficient to maintain good corneal health and on-eye movement during periods of extended wear are unacceptable to produce the innovative extended-wear contact lenses of the present invention.

Preferably, the manufacturing method produces a contact lens having a Dk/t of at least 70 barrers/mm and a Ionoton Ion Permeability Coefficient of at least 0.2×10^{-6} cm²/sec. More preferably, the manufacturing method produces a contact lens having a Dk/t of at least 75 barrers/mm and a Ionoton Ion Permeability Coefficient of at least 0.3×10^{-6} cm²/sec. The manufacturing method preferably provides a contact lens having a Dk/t of at least 87 barrers/mm and a Ionoton Ion Permeability Coefficient of at least 0.4×10^{-6} cm²/sec.

The previous disclosure will enable one having ordinary skill in the art to practice the invention. In order to better enable the reader to understand specific embodiments and the advantages thereof, reference to the following examples is suggested. However, the following examples should not be read to limit the scope of the invention.

Examples A–D are arranged in accordance with the materials defined above. Thus, Examples A-1, A-2, etc. relate to Material “A” as defined above, Examples B-1, B-2, etc. relate to Material “B” as defined above, Examples C-1, C-2, etc. relate to Material “C” and Examples D-1, D-2, etc. relate to Material “D”. Temperatures are stated in degrees Celsius unless otherwise specified.

Examples E, F and G are directed to demonstrating a correlation between on-eye movement and the Ionoton Ion Permeability Coefficient, the Ionoflux Ion Permeability Coefficient, and the Hydrodell Water Permeability Coefficient, respectively.

EXAMPLE A-1

A polysiloxane macromer is prepared by reacting, at room temperature (about 21 C.), one mole equivalent (about 100 grams) of poly(dimethylsiloxane) dialkanol (Shin Etsu Chemical Co., Tokyo, Japan) having hydroxyethyl propoxy end groups with 2 mole equivalents (about 21.2 grams) of isophorone diisocyanate (Aldrich Chemical Co., Milwaukee, Wis.) in the presence of about 0.2 grams dibutyltin dilaurate catalyst (Pfaltz & Bauer, Inc., Waterbury, Conn.). After about 48 hours reaction time, 2.02 mole equivalents (about 38.7 grams) of poly(ethylene glycol) (“PEG” about 610 g/mol Mn, Dow Chemical Corp., Midland, Mich.) and about 0.17 grams of dibutyltin dilaurate (about 0.43% by weight PEG) are added to 80 grams of the reaction product from the prior step. Sufficient chloroform (Aldrich Chemical Co.) is added to the mixture to make the mixture homogeneous. This mixture is stirred at room temperature for about 15 hours. Next, the mixture is stirred for about 8 hours at a temperature of about 44 to 48 C., with the temperature held substantially constant by a surrounding oil bath. The chloroform is then evaporated, in order to achieve a final concentration of about 50% by weight solids, by stirring the mixture at room temperature for about 8 hours. Then, about 2.14 mole equivalents (about 10.4 grams) of isocyanatoethyl methacrylate (“IEM” Monomer Polymer, Inc., Feasterville, Pa.) is added to the mixture. Finally, the mixture is covered with aluminum foil and stirred at room temperature for about 17 hours, yielding a polysiloxane-containing macromer having a number-average molecular weight (Mn) of about 4000 grams per mole.

US 6,951,894 B1

47

The macromeric solution is then polymerized, in the presence of about 0.5 weight percent DAROCUR® 173 photoinitiator (Ciba-Geigy Corporation, Ardsley, N.Y.) to form contact lenses. Polypropylene contact lens molds are filled with the copolymer precursor solution. Ultraviolet light (about 300 to 400 nm) at about 3–6 mW/cm² is applied to the solution in the mold for about 3 hours at room temperature. The UV light, in conjunction with the photoinitiator, causes polymerization, thereby allowing the solution to form a contact lens having the shape of the mold. The lenses are extracted with isopropanol to remove the remaining chloroform solvent and any unreacted components. The product is a polysiloxane-containing polymeric contact lens.

Prior to taking oxygen permeability measurements, the lenses are hydrated by placing the lenses in isotonic buffered saline solution for at least eight hours. After hydration, if necessary because of handling, each lens is cleaned with MIRAFLUX® Daily Cleaner (CIBA Vision Corporation, Duluth, Ga.) to remove grease and lipids prior to testing. Excess MIRAFLUX® cleaner is removed by rinsing with saline or purified water.

Oxygen fluxes (J) are measured at 34 C. in a wet cell (i.e., gas streams are maintained at about 100% relative humidity) using a Dk1000 instrument. Oxygen transmissibility, D_k/t, is determined as outlined in the portions of the specification relating to oxygen permeability and transmissibility.

EXAMPLE A-2

A polysiloxane macromer is first prepared substantially in accordance with the procedure described in Example A-1.

A copolymer precursor solution is prepared by mixing about 180 grams polysiloxane-containing macromer, about 15 grams 3-methacryloxypropyltris (trimethylsiloxy) silane (Shin Etsu), about 4 grams 2-hydroxyethyl methacrylate ("HEMA"), about one gram ethylene glycol dimethacrylate ("EDGMA"), and about one gram DAROCUR® 1173 photoinitiator at room temperature for about 16 hours.

The copolymer precursor solution is then polymerized to form contact lenses. Polypropylene contact lens molds are filled with the copolymer precursor solution. Ultraviolet light (about 300 to 400 nm) at about 3–6 mW/cm² is applied to the solution in the mold for about 3 hours at room temperature. The UV light causes polymerization, thereby allowing the solution to form a contact lens having the shape of the mold. The lens is extracted with isopropanol to remove remaining chloroform solvent and any unreacted components. A preferred resulting polymer contains about 81.8 weight percent polysiloxane macromer, about 13.6% TRIS, about 3.6% 2-hydroxyethyl methacrylate, and about 0.9% EDGMA. [059–87]

The contact lens is degassed by placing the lens under suitable vacuum for a period sufficient to remove substantially all gas from the lens matrix. Fully hydrated degassed contact lenses having this composition have a Dk of about 87 barrers, a water content of about 19 weight percent, and a modulus of elasticity of about 2.5 MPa.

EXAMPLE A-3

A contact lens is prepared substantially in accordance with the procedure described in Example A-2, but having the final composition of about 19.5 weight percent polysiloxane macromer, about 47% TRIS, and about 33.5% N,N-dimethylacrylamide. Fully hydrated contact lenses having this composition have a Dk of about 49 barrers, a water

48

content of about 30 weight percent, and a modulus of elasticity of about 2.4 MPa.

EXAMPLE A-4

A contact lens is prepared substantially in accordance with the procedure described in Example A-2, but having the final composition of about 30 weight percent polysiloxane macromer, about 50% TRIS and about 20% N,N-dimethylacrylamide. Fully hydrated contact lenses having this composition have a Dk of about 76 barrers, a water content of about 20 weight percent, and a modulus of elasticity of about 1.3 MPa.

EXAMPLE A-5

A contact lens is prepared substantially in accordance with the procedure described in Example A-2, but having the final composition of about 30 weight percent polysiloxane macromer, about 40% TRIS and about 30% N,N-dimethylacrylamide. Fully hydrated contact lenses having this composition have a Dk of about 55 barrers, a water content of about 30 weight percent, and a modulus of elasticity of about 3.5 MPa.

EXAMPLE A-6

A contact lens is prepared substantially in accordance with the procedure described in Example A-2, but having the final composition of about 30 weight percent polysiloxane macromer, about 60% TRIS and about 10% N,N-dimethylacrylamide. Fully hydrated contact lenses having this composition have a Dk of about 110 barrers, a water content of about 8.7 weight percent, and a modulus of elasticity of about 2.6 MPa.

EXAMPLE A-7

A contact lens is prepared substantially in accordance with the procedure described in Example A-2, but having the final composition of about 30 weight percent polysiloxane macromer and about 70% TRIS. Fully hydrated contact lenses having this composition have a Dk of about 128 barrers and a water content of about 4.9 weight percent.

EXAMPLE A-8

A contact lens is prepared substantially in accordance with the procedure described in Example A-2, but having the final composition of about 30 weight percent polysiloxane macromer, about 45% TRIS, 5% fluoroacrylate, and about 20% N,N-dimethylacrylamide. Fully hydrated contact lenses having this composition have a Dk of about 69 barrers, a water content of about 20 weight percent, and a modulus of elasticity of about 1.4 MPa.

EXAMPLE A-9

A contact lens is prepared substantially in accordance with the procedure described in Example A-2, but having the final composition of about 82 weight percent polysiloxane macromer, about 14.4% TRIS, and about 3.7% 2-hydroxyethyl methacrylate. Fully hydrated contact lenses having this composition have a Dk of about 96 barrers, a water content of about 19 weight percent, and a modulus of elasticity of about 1.8 MPa.

EXAMPLE A-10

A polysiloxane macromer is prepared substantially in accordance with the procedures described in Example A-1, but the polyethylene glycol has a molecular weight of about 660.

US 6,951,894 B1

49

A contact lens is prepared substantially in accordance with the procedure described in Example 2, but having the final composition of about 81.9 weight percent polysiloxane macromer, about 13.6% TRIS, about 3.7% 2-hydroxyethyl methacrylate, and about 0.8% ethylene glycol dimethacrylate. Fully hydrated contact lenses having this composition have a Dk of about 81 barrers, a water content of about 20 weight percent, and a modulus of elasticity of about 1.4 MPa.

EXAMPLE A-11

A contact lens is prepared substantially in accordance with the procedure described in Example A-2, but having the final composition of about 82 weight percent polysiloxane macromer, about 8.6% TRIS, about 4.9% fluoroacrylate, about 3.5% 2-hydroxyethyl methacrylate, and about 1% EDGMA. Fully hydrated contact lenses having this composition have a Dk of about 77 barrers, a water content of about 22 weight percent, and a modulus of elasticity of about 1.3 MPa.

EXAMPLE A-12

A contact lens is prepared substantially in accordance with the procedure described in Example A-1, but the polysiloxane macromer used has hydroxy-sec-butyl end groups as opposed to hydroxyethylpropoxy end groups. The fully hydrated contact lens, after degassing, has a Dk of about 70 barrers, about a 22 weight percent water content, and a modulus of elasticity of about 2.4 MPa.

EXAMPLE B-1

Macromer Synthesis

51.5 g (50 mmol) of the perfluoropolyether Fomblin® ZDOL (from Ausimont S.p.A, Milan) having a mean molecular weight of 1030 g/mol and containing 1.96 meq/g of hydroxyl groups according to end-group titration is introduced into a three-neck flask together with 50 mg of dibutyltin dilaurate. The flask contents are evacuated to about 20 mbar with stirring and subsequently decompressed with argon. This operation is repeated twice. 22.2 g (0.1 mol) of freshly distilled isophorone diisocyanate kept under argon are subsequently added in a counterstream of argon. The temperature in the flask is kept below 30° C. by cooling with a waterbath. After stirring overnight at room temperature, the reaction is complete. Isocyanate titration gives an NCO content of 1.40 meq/g (theory: 1.35 meq/g).

202 g of the α,ω -hydroxypropyl-terminated polydimethylsiloxane KF-6001 from Shin-Etsu having a mean molecular weight of 2000 g/mol (1.00 meq/g of hydroxyl groups according to titration) are introduced into a flask. The flask contents are evacuated to approx. 0.1 mbar and decompressed with argon. This operation is repeated twice. The degassed siloxane is dissolved in 202 ml of freshly distilled toluene kept under argon, and 100 mg of dibutyltin dilaurate (DBTDL) are added. After complete homogenization of the solution, all the perfluoropolyether reacted with isophorone diisocyanate (IPDI) is added under argon. After stirring overnight at room temperature, the reaction is complete. The solvent is stripped off under a high vacuum at room temperature. Microtitration shows 0.36 meq/g of hydroxyl groups (theory 0.37 meq/g). 13.78 g (88.9 mmol) of 2-isocyanatoethyl methacrylate (IEM) are added under argon to 247 g of the α,ω -hydroxypropyl-terminated polysiloxane-perfluoropolyether-polysiloxane three-block copolymer (a three-block copolymer on stoichiometric

50

average, but other block lengths are also present). The mixture is stirred at room temperature for three days. Microtitration then no longer shows any isocyanate groups (detection limit 0.01 meq/g). 0.34 meq/g of methacryl groups are found (theory 0.34 meq/g).

The macromer prepared in this way is completely colourless and clear. It can be stored in air at room temperature for several months in the absence of light without any change in molecular weight.

EXAMPLE B-2

Macromer Synthesis

The first step of the macromer synthesis described under Example B-1 is repeated. An isocyanate titration of the perfluoropolyether reacted with IPDI gives a content of 1.33 meq/g of NCO (theory 1.35 meq/g).

In a second step, 87.1 g of the α,ω -hydroxypropyl-terminated polydimethylsiloxane TegomerH-Si2111 (Th. Goldschmidt AG, Essen) having a mean molecular weight of 890 g/mol (2.25 meq/g of hydroxyl groups according to titration) are dissolved in 87 ml of toluene. After the reaction has been carried out as indicated under B-1 and the solvent has been removed, a hydroxyl group content of 0.66 meq/g is determined by microtitration (theory 0.60 meq/g). The resultant intermediate is in turn reacted with a stoichiometric amount of isocyanatoethyl methacrylate. Microtitration then no longer shows any isocyanate groups (detection limit 0.01 meq/g). 0.56 meq/g of methacryl groups are found (theory 0.53 meq/g). The macromer prepared in this way is completely colourless and clear and has a long shelf life.

EXAMPLE B-3

Macromer Synthesis

The first step of the macromer synthesis described under Example B-1 is repeated, but using a different perfluoropolyether: Fomblin® ZDOLTX (from Ausimont S.p.A., Milan). This material is terminated by $\text{O}-\text{CF}_2-\text{CH}_2-(\text{OCH}_2\text{CH}_2)_n-\text{OH}$ (where $n=0, 1$ or 2). The material used has a mean molecular weight of 1146 g/mol, and contains 1.72 meq/g of hydroxyl groups according to end-group analysis. An isocyanate titration of the perfluoropolyether reacted with IPDI shows a content of 1.23 meq/g of NCO (theory 1.25 meq/g).

In the second step, a stoichiometric amount of Tegomer Hi-Si211 and toluene are again added. After the reaction has been carried out as indicated under Example B-1 and the solvent has been removed, a hydroxyl group content of 0.63 meq/g is determined by microtitration (theory 0.58 meq/g). The resultant intermediate is in turn reacted with a stoichiometric amount of isocyanatoethyl methacrylate. Microtitration then no longer shows any isocyanate groups (detection limit 0.01 meq/g). 0.55 meq/g of methacryl groups are found (theory 0.51 meq/g). The macromer prepared in this way is completely colourless and clear and has a long shelf life.

EXAMPLE B-4

Macromer Synthesis

The first step of the macromer synthesis described under Example B-1 is repeated, but 5.0 g of Fomblin/ZDOL and 2.18 g of IPDI are employed. When the reaction is complete, microtitration shows an isocyanate group content of 1.31 meq/g of hydroxyl groups (theory 1.36 meq/g).

The second step of the synthesis described under Example B-1 is likewise carried out analogously, the stoichiometric